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RELATION OF ENDOCRINE DISTURBANCES TO CERTAIN HEREDODEGENERATIVE SYMPTOMS

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The remarkable increase in the knowledge of the physiology and functions of the glands of internal secretion has not been accompanied by corresponding progress in clinical endocrinology. There are several reasons for this. One is the fact that the experimental physiologist is working with a uniform stock of animals, which are presumably identical in their inherited characteristics. The clinical endocrinologist, on the other hand, is dealing with patients of quite different origin and somatic make-up. It is well known that endocrine diseases are often found in persons who also show nonendocrine deviations from the normal; that is, changes that are usually but inappropriately termed stigmas of degeneration.[1] It is therefore difficult to determine whether all of the accompanying symptoms are the result of, the cause of or merely independently coincident with the endocrine condition.

There can be mentioned at least three errors into which one might fall in attempting to determine the causal connection between endocrine symptoms and those which belong in another category. First, the abnormal endocrine condition could be considered, correctly or not, as the cause of the accompanying symptoms. Second, the accompanying symptoms could be considered as the cause of the endocrine dysfunction. Third, in a patient showing two abnormal endocrine conditions, one could be considered the cause of the other. To illustrate these three possibilities examples will be cited, and it will be discussed whether or

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1. (*a*) Bauer, Julius: Konstitutionelle Disposition zu inneren Krankheiten, ed. 3, Berlin, Julius Springer, 1924. (*b*) Pfaundler, Meinhard: Constitution and Constitutional Anomalies, in von Pfaundler, M., and Schlossmann, A.: Diseases of Children, translated by M. G. Peterman, ed. 4, J. B. Lippincott Company, 1935, vol. 2.

not the two abnormal conditions stand in any causal relation to each other. If such a connection does not exist, it may be argued that they are merely coordinated independent deviations from the norm, possibly caused by damage to the germ plasm in the immediate or in some previous ancestral generation.

ENDOCRINOPATHY THOUGHT TO BE THE CAUSE OF AN ACCOMPANYING ABNORMALITY

Examples are the cases in which endocrine disturbances are accompanied by myopathies. For instance, progressive muscular dystrophy combined with abnormalities of the thyroid gland has been noted repeatedly.[2] If an observer happened to encounter several cases of this combination, he might conclude that the myopathy was due to the abnormal functioning of the thyroid gland. However, muscular dystrophy has also been found in combination with Fröhlich's syndrome,[3] infantilism,[4] polyuria and polydipsia,[5] precocious puberty,[6]

2. (*a*) Boveri, cited by Janney, N. W.; Goodhart, S. P., and Isaacson, V. I.: The Endocrine Origin of Muscular Dystrophy, Arch. Int. Med. **21**:188-215 (Feb.) 1918. (*b*) Bramwell, E.: Muscular Dystrophies, Sympathetic System, and Endocrine Glands, Lancet **2**:1103-1109 (Nov. 28) 1925. (*c*) Curschmann, H.: Das endokrine System bei Neuro-, insbesondere Myoneuropathien, Ergebn. d. inn. Med. u. Kinderh. **21**:467-497, 1922. (*d*) Falta, Wilhelm: Die Erkrankungen der Blutdrüsen, Berlin, Julius Springer, 1913, p. 389. (*e*) Maiweg, H.: Progressive Muskeldystrophie und Thyreohypoplasie, Ztschr. f. d. ges. Neurol. u. Psychiat. **63**:107-122, 1921. (*f*) Prager, M.: Casuistische Beiträge zur Kenntnis der Dystrophia muscularis progressiva (Erlangen), Fürth, A. Schröder, 1891. (*g*) Rohr, F.: Progressive Muskeldystrophie und endokrine Drüsen, Med. Klin. **19**:903, 1923. (*h*) Schenk, P., and Mathias, E.: Zur Kasuistik der Dystrophia musculorum progressiva retrahens, Berl. klin. Wchnschr. **57**:557-558, 1920. (*i*) Schlesinger, cited by Oppenheim, H.: Lehrbuch der Nervenkrankheiten, Berlin, S. Karger, 1908, vol. 1, p. 286. (*j*) von Werdt, F.: Ein Fall von Dystrophia musculorum progressiva mit Sektionsbefund, Frankf. Ztschr. f. Path. **2**:577-590, 1908-1909.

3. (*a*) Bramwell.[2b] (*b*) Brock, S., and Kay, W. E.: Study of Unusual Endocrine Disturbances: Their Associated Myopathies, Endocrine Balance and Metabolism Findings, Arch. Int. Med. **27**:1-37 (Jan.) 1921. (*c*) von Dziembowski, S.: Dystrophia adiposogenitalis mit Myopathie, Deutsche med. Wchnschr. **43**:654, 1917. (*d*) Foerster, O., cited by Bramwell.[2b] (*e*) Fränkel, F.: Die Beziehungen der progressiven Muskeldystrophie zu den Erkrankungen der Blutdrüsen, Ztschr. f. d. ges. Neurol. u. Psychiat. **78**:283-290, 1922. (*f*) Gareiso, A.; Obarrio, J. M., and Prete, A. J.: Sindrome adiposogenital de Babinski-Fröhlich con adiposidad dolorosa y miopatia, Prensa méd. argent. **19**:1224-1230 (Dec. 20) 1932. (*g*) Landé, L.: Infantile Dystrophia musculorum progressiva, kombiniert mit Dystrophia adiposo-genitalis, Ztschr. f. Kinderh. **42**:355-360, 1926. (*h*) McCouch, G. P., and Ludlum, S. D. W.: Is Myopathy Related to Disorders of Internal Secretions? M. Rec. **89**:1042-1046, 1916. (*i*) Riggs, C. E.: Endocrinic Type of Muscular Dystrophy, Minnesota Med. **9**:98, 1926. (*j*) Schaefer, V.: Dystrophia adiposo-genitalis und Dystrophia musculorum progressiva als Nachkrankheiten der Poliomyelitis anterior acuta, Deutsche Ztschr. f. Nervenh. **126**:285-293, 1932.

(*Footnotes continued on next page*)

tumors of the pituitary gland,[7] and hypoglycemia.[8] Timme [9] stated the belief that progressive muscular dystrophy is an endocrine disease, chiefly because the roentgenograms revealed shadows in the region of the pineal gland—an insufficient reason. Pathologic changes in the thymus were found by Goodhart and Globus.[8b] It hardly appears probable, therefore, that muscular dystrophy is the result of a pathologic disturbance of any one endocrine gland. A similar situation exists when muscular hypertrophy is found in combination with endocrinopathies. An athletic appearance of certain persons with hypothyroidism has been repeatedly pointed out.[10] An unusual degree of muscular strength has been seen in conjunction with dystrophia adiposogenitalis (fig. 1 *A*).[3b] Obesity was also present in the interesting family described by Barnes,[11] some members of which had hypertrophic and other

4. Bramwell.[2b] Falta.[2d] Barker, L. F.: Discussion of Five Patients Exhibiting Certain Forms of Muscular Wasting (Progressive Central Muscular Atrophy and Progressive Muscular Dystrophy), M. Clin. North America **14**:109-125, 1930. Friedreich, N.: Ueber progressive Muskelatrophie, über wahre und falsche Muskelhypertrophie, Berlin, A. Hirschwald, 1873. De Nicolò, F.: Ricerche semeiologiche endocriniche su di un caso di distrofia muscolare progressiva (tipo Duchenne), Pediatria **34**:1014-1023, 1926. Wright, C.: Progressive Muscular Dystrophy with Pseudohypertrophy from Endocrine Standpoint, California & West. Med. **23**:999-1002, 1925.

5. Flinker, R.: Ein Fall von Dystrophia musculorum progressiva mit Polyurie und Polydipsie, Deutsche Ztschr. f. Nervenh. **135**:71-73, 1934.

6. Janney, N. W.; Goodhart, S. P., and Isaacson, V. I.: The Endocrine Origin of Muscular Dystrophy, Arch. Int. Med. **21**:188-215 (Feb.) 1918.

7. Marburg, O.: Ueber das basophile Adenom der Hypophyse, die zerebrale Fettsucht und die Pseudohypertrophie der Muskeln, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **35**:143-160, 1933. Clark and Atwood, cited by Lewandowsky, M. H.: Handbuch der Neurologie, Berlin, Julius Springer, 1910-1919, vol. 4, p. 247.

8. (*a*) Janney and others.[6] (*b*) Goodhart, S. P., and Globus, J. H.: On the Nature of Muscular Dystrophies, with a Report of Changes in Cardiac Muscle in Two Cases, Neurol. Bull. **1**:386-390, 1918. (*c*) McCrudden, F. H.: The Nature of the Pathologic Process in Progressive Muscular Dystrophy, Arch. Int. Med. **21**:256-262 (Feb.) 1918.

9. Timme, W.: Progressive Muscular Dystrophy as an Endocrine Disease, Arch. Int. Med. **19**:79-104 (Jan.) 1917.

10. Debré, R., and Sémelaigne, G.: Syndrome of Diffuse Muscular Hypertrophy in Infants Causing Athletic Appearance: Its Connection with Congenital Myxedema, Am. J. Dis. Child. **50**:1351-1361 (Dec.) 1935. Langhans, T.: Anatomische Beiträge zur Kenntnis der Cretinen (Knochen, Geschlechtsdrüsen, Muskeln und Muskelnspindeln, nebst Bemerkungen über die physiologische Bedeutung der letzteren), Virchows Arch. f. path. Anat. **149**:155-187, 1897. Pfaundler, M., in Feer, E.: Lehrbuch der Kinderheilkunde, Jena, Gustav Fischer, 1922, p. 202. Wieland, E., in von Pfaundler, M., and Schlossmann, A.: Handbuch der Kinderheilkunde, ed. 4, Leipzig, F. C. W. Vogel, 1931, vol. 1, p. 1225.

11. Barnes, S.: Myopathic Family, with Hypertrophic, Pseudohypertrophic, Atrophic and Terminal (Distal in Upper Extremities) Stages, Brain **55**:1-46, 1932.

members atrophic myopathies. Most of the persons in this family passed from a hypertrophic stage through a pseudohypertrophic stage into an atrophic state. A member of this family is seen in figures 1 *B* and *C*. This man, who shows obesity, like many other members of the family, was in his youth "capable of lifting from the floor a 56 lb. weight between the thumb and finger of either hand. He could climb a flight of stairs with a load of 500 lbs. on his back. About 1906 he attended a fair where a performing bear was wrestling with his

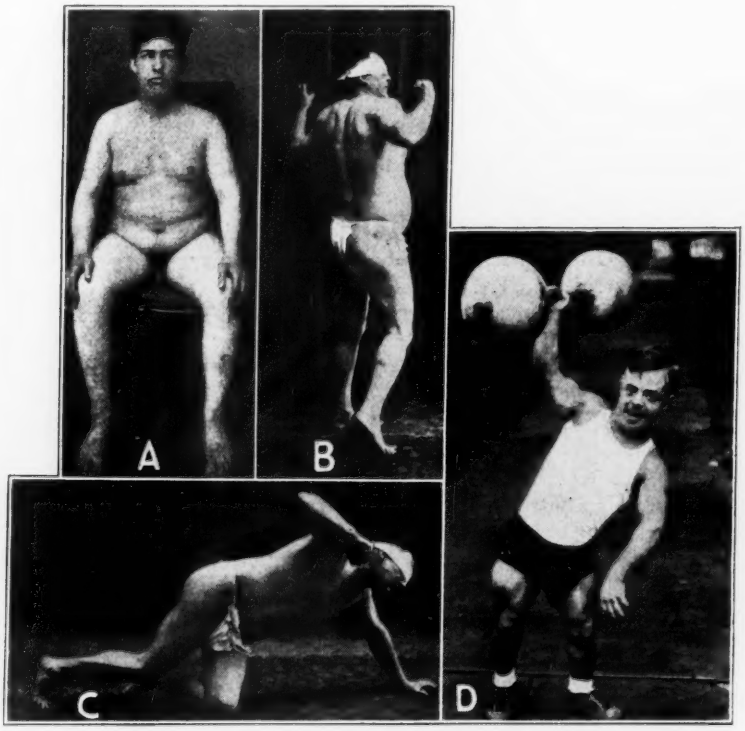

Fig. 1.—*A*, from Brock and Kay,[3b] shows an unusual degree of muscular strength in combination with dystrophia adiposogenitalis. *B* and *C*, from Barnes,[11] show muscular hypertrophy and obesity. *D* shows muscular hypertrophy, possibly associated with adrenal tumor.[13]

keeper; in response to a challenge he stepped forward, wrestled with the bear and laid it out! Realizing his great physical capacity, he became a furniture mover, and acquired both profit and pleasure in exhibiting his colossal lifting powers; but during the last twenty years the power of his legs steadily diminished" and a pseudohypertrophic muscular dystrophy of the legs developed. Abnormal muscular strength in children with tumors of the adrenal cortex is a well known

symptom.[12] Persons with this condition are said to be of the Hercules type. Figure 1 *D* shows a boy of 11 years of age with remarkable muscular development.[13] This lad, according to the history, at the age of 2½ years was out in his family's Ford automobile. A flat tire disclosed the fact that no jack was available. In spite of his tender years the boy held up the car while the tire was being replaced. At

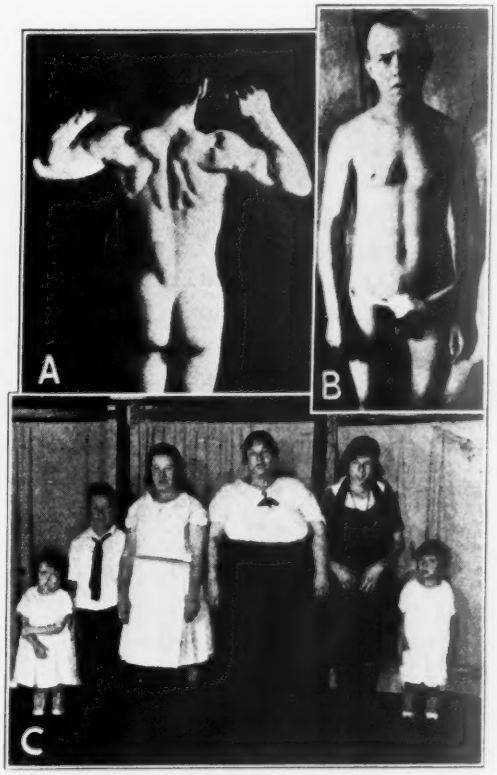

Fig. 2.—*A*, from Horrax (1937),[14] illustrates muscular hypertrophy associated with pinealoma. *B*, from Brock and Kay,[3b] shows congenital myotonia associated with hypothyroidism. *C*, from Rosett,[15] shows a family with myotonia, some members of which have obesity.

12. Adams, C. E.: A Case of Precocious Development Associated with a Tumour of the Left Suprarenal Body, Tr. Path. Soc. London **56**:208-212, 1905. Ambrožič, M., and Baar, H.: Ein Fall von Makrogenitosomia praecox und Nebennierentumor bei einem 3 jährigen Mädchen, Ztschr. f. Kinderh. **27**:135-152, 1921. Jump, H. D.; Beates, H., Jr., and Babcock, W. W.: Precocious Development of the External Genitals Due to Hypernephroma of the Adrenal Cortex, Am. J. M. Sc. **147**:568-574, 1914.

13. This photograph is shown through the courtesy of Dr. Teter of Toledo, Ohio.

about 3½ or 4 years of age he began to shave; he continued to develop, performing feats of great muscular strength. In roentgenograms of the head no lesions were seen in the pituitary or pineal region. That fact and the absence of symptoms of increased intracranial pressure indicated that a pineal tumor was unlikely and suggested instead the probability of a tumor of the adrenal cortex, although the clinical differentiation between these two types of tumor is often difficult.

A high degree of muscular development was seen by Horrax in a boy 10 years old (fig. 2 *A*) in whom a pinealoma was shown in a roentgenogram and verified by operation.[14]

Such reports of cases of muscular hypertrophy combined with disturbances of the thyroid, pituitary, adrenal or pineal gland make it impossible to attribute the condition to any one of the glands mentioned.

The situation is similar in the case of myotonia congenita (Thomsen's disease), which should not be confused with myotonia atrophica. Congenital myotonia may be accompanied by signs of cretinism or goiter as well as by testicular atrophy, as in the case reported by Brock and Kay (fig. 2 *B*).[3b] In a family exhibiting the same disease, studied by Rosett,[15] some members showed definite signs of obesity (fig. 2 *C*). A case of hypertrophic—though not congenital—myotonia was recently reported by Garcin and his co-workers (fig. 3 *A* and *B*).[16] The basal metabolic rate in this case was —33 per cent.

The same difficulties are encountered if one attempts to subordinate etiologically to endocrine disturbances certain changes in the bones. It has sometimes been suggested[17] that osteogenesis imperfecta and osteopsathyrosis idiopathica, both characterized by generalized fragilitas ossium, are caused by endocrine disturbances. Osteogenesis imperfecta has been found in association with lesions of the parathyroid glands,[18]

14. Horrax, G.: Further Observations on Tumor of the Pineal Body, Arch. Neurol. & Psychiat. **35**:215-228 (Feb.) 1936; Extirpation of a Huge Pinealoma from a Patient with Pubertas Praecox: A New Operative Approach, ibid. **37**: 385-397 (Feb.) 1937. Zondek, H.: Diseases of the Endocrine Glands, ed. 3, Baltimore, William Wood & Company, 1935, p. 926.

15. Rosett, J.: Thomsen's Disease, Brain **45**:1-30, 1922.

16. Garcin, R.; Rouques, L.; Laudat, and Frumusan, P.: Syndrome thomsénien et syndrome myxoedémateux cliniquement associés. Début simultané et évolution parallèle: Etude clinique, Rev. neurol. **64**:59-72, 1935.

17. Kienböck, R.: Ueber infantile Osteopsathyrose, Fortschr. a. d. Geb. d. Röntgenstrahlen **23**:122-168, 1915. Fahr, T.: Ueber Osteogenesis imperfecta, Virchows Arch. f. path. Anat. **261**:732-750, 1926. Ewald, P.: Ueber Osteopsathyrosis idiopathica, Ztschr. f. orthop. Chir. **33**:634-646, 1913.

18. Wyatt, T. C., and McEachern, T. H.: Congenital Bone Dysplasia (Osteogenesis Imperfecta) Associated with Lesions of Parathyroid Glands, Am. J. Dis. Child. **43**:403-415 (Feb.) 1932.

with an abnormally small thymus[19] and with an abnormally large thyroid gland.[20] Osteopsathyrosis has been seen in obese and dwarfed persons (fig. 3 *C*).[21] It has been observed also in combination with glycosuria,[22] with disturbances of the thyroid[23] and of the parathyroid glands,[24] with pubertas praecox[25] and with hypogenitalism.[26]

The combination of these osseous diseases with abnormalities of the endocrine glands is, however, the exception. A greater number of cases occur in which the endocrine findings are normal, and a causal relationship has been denied repeatedly.[27]

Engelbach and Schaefer[28] have observed osteochondritis or epiphysitis in conjunction with pituitary dwarfism. Since the fuzzy, ragged appearance of the epiphyses and osseous centers vanished after administration of an extract containing the growth hormone (fig. 3 *D*), these authors suggested the possibility that Köhler's disease, Perthes' disease and the like are due to an incretory imbalance. It should not be forgotten, however, that other forms of pathologic change in bones and deformities of the skeleton are frequently found together with

19. Keene, M. F. L.: Osteogenesis Imperfecta, Lancet **2**:661 (Sept. 23) 1922. Frontali, G.: Fragilità ossea congenita e timo (contributo allo studio delle distrofie ossee in rapporto con le glandole endocrine), Riv. di clin. pediat. **18**:258-309, 1920.

20. Niklas, F.: Osteogenesis imperfecta, Beitr. z. path. Anat. u. z. allg. Path. **61**:101-130, 1915.

21. (*a*) Hartmann, J.: Zur Frage der Osteopsathyrosis idiopathica, Deutsche Ztschr. f. Chir. **111**:383-412, 1911. (*b*) Hart, C.: Ueber die anatomische Grundlage der Osteopsathyrosis idiopathica insbesondere die Osteogenesis imperfecta, Beitr. z. path. Anat. u. z. allg. Path. **59**:207-275, 1914.

22. Bowcock, H. M., and Lewis, G. T.: Brittle Bones and Blue Sclerae: Report of Case with Glycosuria, Ann. Int. Med. **3**:700-706, 1930.

23. Zesas, D. G.: Beitrag zur Pathologie der idiopathischen Osteopsathyrose, Deutsche Ztschr. f. Chir. **123**:380-404, 1913. Terrien, F.; Sainton, P., and Veil, P.: Deux cas de syndrome de Van der Hoeve (oeil blue; fragilité osseuse; surdité), Arch. d'opht. **44**:293-301, 1927. Gutzeit, R.: Ueber blaue Sklera und Knochenbrüchigkeit, Klin. Monatsbl. f. Augenh. **68**:771-774, 1922.

24. Takahashi, T.: Beitrag zur Kenntnis der blauen Sclera, Arch. f. Ophth. **115**:206-214, 1924.

25. Meissner, R.: Ueber Beziehungen von Osteopsathyrosis idiopathica zum endokrinen System, Med. Klin. **18**:1397-1400, 1922.

26. Wagoner, G. W.: Idiopathic Osteopsathyrosis, Ann. Surg. **80**:115-123, 1924.

27. Bauer,[1a] Sumita, M.: Ueber die angebliche Bedeutung von Schilddrüsenveränderungen bei Chondrodystrophia foetalis und Osteogenesis imperfecta, Jahrb. f. Kinderh. **73**:50-84, 1911. Kraus, E. J.: Osteogenesis imperfecta und endokrines System, Virchows Arch. f. path. Anat. **274**:37-49, 1929. Ther, L.: Ist die Osteogenesis imperfecta ein endokrines Leiden? ibid. **295**:57-64, 1935.

28. Engelbach, W., and Schaefer, R. L.: Endocrine Dwarfism, J. A. M. A. **103**:464-468 (Aug. 18) 1934.

endocrinopathies in one person. Thus obesity and Morquio's disease were seen together in a child (fig. 4 *A* and *B*).[29] It is unlikely that there is a causal connection, since it is known that Morquio's disease, which, as we have reported elsewhere,[30] is probably an atypical chondrodystrophy, is usually found in children who have no sign of endocrine disturbance. If, finally, acrocephaly, polydactylism, syndactylism, genu valgum, dislocation of the patella and various other

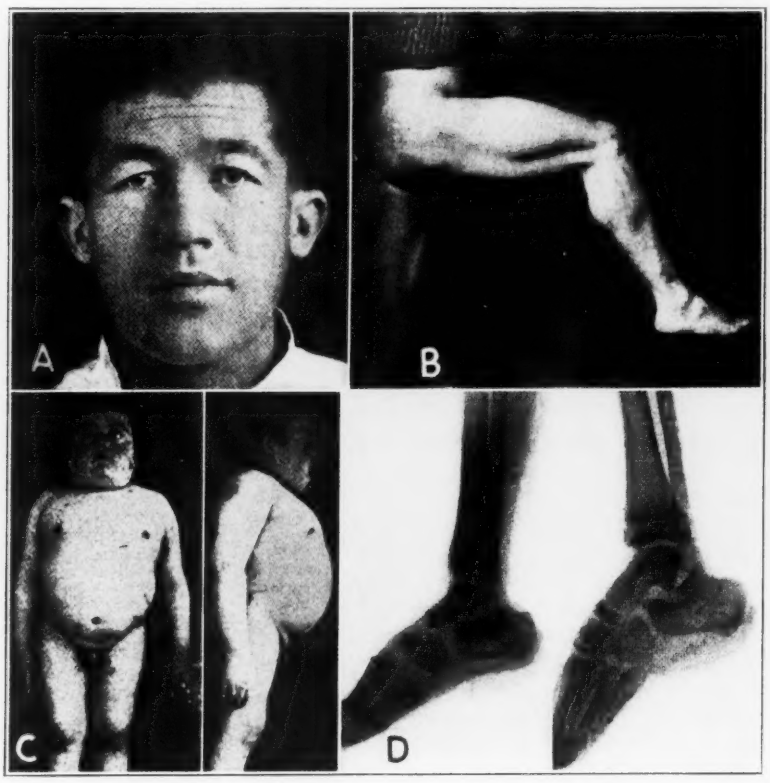

Fig. 3.—*A*, from Garcin,[16] illustrates myotonia and myxedema. *B* shows the leg of the same patient. *C*, from Hart,[21b] shows osteopsathyrosis and obesity, and *D*, from Engelbach and Schaefer,[28] roentgenograms made in a case of osteochondritis, (left) before and (right) after treatment with growth hormone.

skeletal deformities are combined with obesity and hypogenitalism in a patient (fig. 4 *C*), one cannot think seriously that these deformities are due to an endocrine imbalance.

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29. Grenet, H.; Lévesque, J., and Isaac-Georges, P.: Obésité, nanisme et dystrophies osseuses multiples, Bull. Soc. de pédiat. de Paris **32**:79-85, 1934.

30. Warkany, J., and Mitchell, A. G.: Atypical Chondrodystrophy, J. Pediat. **4**:734-745, 1934.

These examples demonstrate that a great variety of diseases of the muscular system as well as of the skeleton may be found together with endocrine dysfunction. But since many of these diseases of the muscle or bone are also encountered without endocrine imbalance, a causal relationship can hardly be assumed.

A NONENDOCRINE ABNORMALITY CONSIDERED AS THE CAUSE OF AN ENDOCRINE DYSFUNCTION

This section introduces the subject of infantilism. If a generalized retardation of growth is found combined with polydactylism, hypospadias or deformity of any organ not essentially connected with

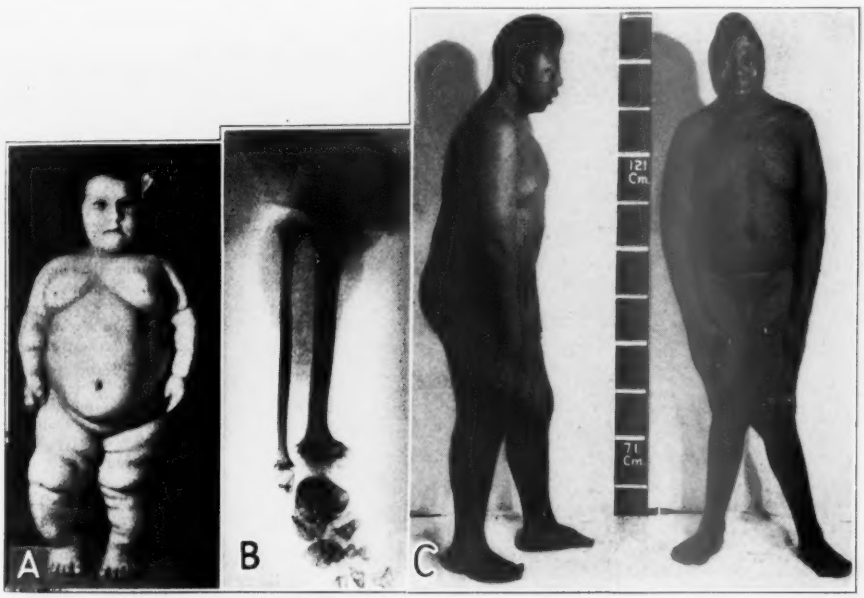

Fig. 4.—*A*, from Grenet and others,[29] illustrates obesity in Morquio's disease. *B* is a roentgenogram of the child shown in *A*. *C* shows obesity in a patient with acrocephalus, polydactylism, syndactylism, genu valgum and other skeletal deformities.

metabolism, the two conditions are usually considered independent deviations. However, if an organ like the kidney or the liver is abnormal, the stunted growth is commonly thought to be secondary to the renal or hepatic deficiency and may at times be spoken of as renal or hepatic infantilism, as the case may be. Renal infantilism (without rickets) is especially difficult to analyze. It is true that an obstructive deformity or chronic infection of the urinary tract will lead to inhibition of development and growth. If surgical help is possible, improvement

in this retarded state may occur after removal of the obstruction or of the infected organ. In such a case the infantilism or dwarfism is probably not primarly due to an endocrine disturbance, although the pituitary or other endocrine glands may be secondarily affected and thus contribute to failure of development. However, some authors have expressed the belief that the dwarfism in these cases is primarily caused by an endocrine disturbance, a point of view supported by the fact that in some cases dwarfism is associated with obesity,[31] with an abnormal development of the genitalia [32] or with diabetes mellitus.[33]

The belief that dwarfism in some of these cases is not caused by renal insufficiency obtains support from the fact that a few children who show renal dwarfism in later life have a surprisingly low weight at birth, although they show signs of maturity.[34] This observation, as well as the fact that the pathologic condition of the kidney which is usually found in so-called renal infantilism is not always accompanied by stunted growth,[35] has led many authors to conclude that chronic interstitial nephritis and infantilism found together in one child are independent conditions due to a common cause, such as injury of the germ plasma or heredity.[36] Observation of other deformities in children with renal dwarfism [37] has supported this view.

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31. Hutinel, V.: Sur une dystrophie spéciale des adolescents: Rachitisme tardif avec impotence musculaire, nanisme, obésité et retard des fonctions génitales, Gaz. d. hôp. **80**:27-32, 1912.

32. Cookson, H. A.: Post-Mortem Findings in a Case of Renal Dwarfism, Brit. M. J. **2**:196-197 (Aug. 4) 1928. Jacob, P., and Durant: Néphrite chronique azotémique de l'adolescence et de l'enfance avec infantilism. L'infantilisme rénal, Gaz. d. hôp. **94**:709-712, 1921. Souques, A., and Castaigne, J.: Contribution à la pathogénie du rhumatisme cérébral, Bull. et mém. Soc. méd. d. hôp. de Paris **16**:565-575, 1899.

33. Fairbank, H. A. T., in discussion on Aschcroft, G. V.: Renal Rickets, J. Bone & Joint Surg. **8**:279-291, 1926.

34. Hamperl, H., and Wallis, K.: Ueber renalen Zwergwuchs ohne und mit (renaler) Rachitis, Ergebn. d. inn. Med. u. Kinderh. **45**:589-642, 1933.

35. Mitchell, A. G.: Nephrosclerosis (Chronic Interstitial Nephritis) in Childhood, with Special Reference to Renal Rickets, Am. J. Dis. Child. **40**:101 (July); 345 (Aug.) 1930.

36. Hamperl and Wallis.[34] Loeschke, A.: Beiträge zur Pathogenese des renalen Zwergwuchses, Jahrb. f. Kinderh. **143**:11-35, 1934.

37. Duken, J.: Beitrag zur Kenntnis der malacischen Erkrankungen des kindlichen Skelettsystems: II. Spätrachitis, Tetanie und chronische Schrumpfniere, Ztschr. f. Kinderh. **46**:137-155, 1928. Naish, A. E.: Infantilism with Chronic Interstitial Nephritis, Brit. J. Child. Dis. **9**:337-343, 1912. Wallis, K.: Ueber eine eigentümliche Kombination des renalen Zwergwuchses mit spastischer Diplegie, Idiotie und Optikusatrophie (Silbersternscher Typus), Monatschr. f. Kinderh. **61**:121-126, 1934.

TWO ENDOCRINE DISTURBANCES THOUGHT TO BE CAUSALLY RELATED

In some subjects one observes at the same time two or more endocrine defects. It might then be assumed that one gland is primarily at fault and the other involved as a consequence. In most cases this assumption would probably be correct. However, certain observations suggest that in some instances there may be parallel deficiencies rather than a primary and a subordinated condition. For example, in some diabetic children treated with insulin dwarfism (fig. 5 *A*) has occured and in others infantilism has been found (fig. 5 *B*). It might be

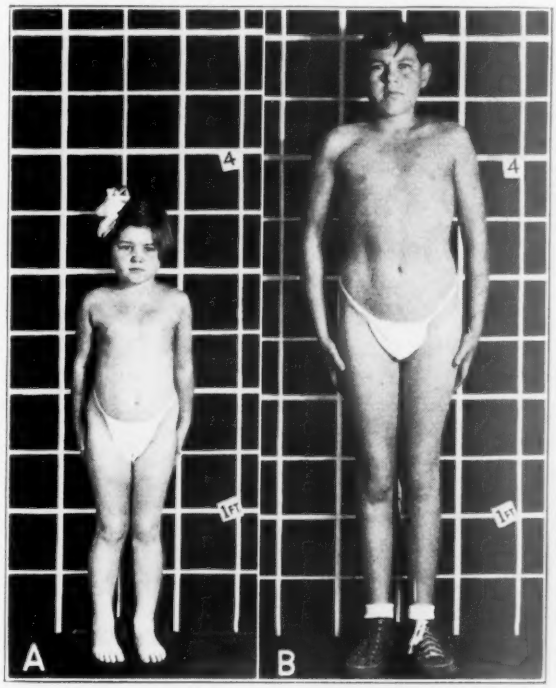

Fig. 5.—*A* shows retarded growth in a diabetic child and *B*, infantilism in a diabetic child. The horizontal lines marked indicate distances of 1 foot and 4 feet from the floor.

assumed that the delay in development in these instances was secondary to the diabetic condition. But in the diabetic clinic of the Children's Hospital of Cincinnati Dr. E. Nelson observed among twenty-seven diabetic patients only four children retarded in growth or development. Gibson and Fowler [38] reported eight cases of severe diabetes mellitus combined with infantilism and proportionate dwarfism and concluded that the

38. Gibson, R. B., and Fowler, W. M.: Infantilism and Diabetes Mellitus, Arch. Int. Med. **57**:695-707 (April) 1936.

dwarfism was not the result of the diabetic condition, since six of these eight patients had received insulin treatment for years. In such cases one may perhaps mistakenly interpret two parallel endocrinopathies as having a cause and effect relationship.

DISCUSSION

One could enlarge on this subject and furnish many examples. However, those given may perhaps suffice to illustrate the clinician's difficulties in the diagnosis and treatment of endocrine malfunction in man. So long as it cannot be determined clearly whether or not the symptoms in a patient are due to endocrine disease, it is obviously impossible to judge the efficacy of hormonal treatment. A thorough

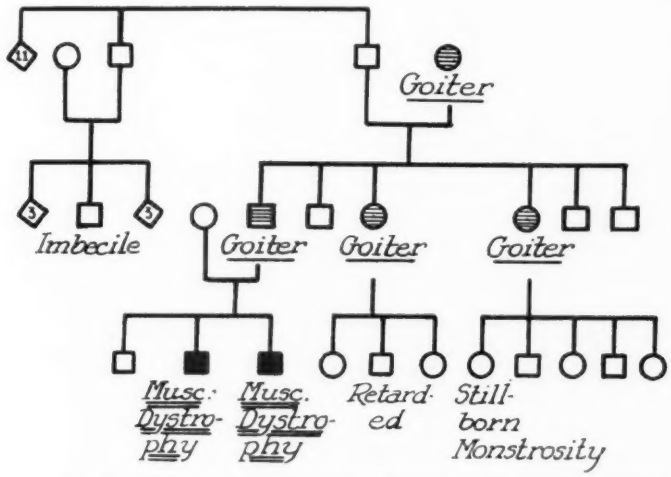

Fig. 6.—Family tree showing muscular dystrophy in some members of the family and goiter in others.

knowledge of the association of heredofamilial deviations, whether they are morphologic or functional, would help greatly in preventing false conclusions.

Some of these endocrine disturbances certainly go back to a faulty intra-uterine development. The factor responsible for the endocrine abnormality might also influence the development of other organs. One can therefore expect a great variety of deviations in such cases. Interesting as it is to study these combinations, we do not advocate premature classifications into syndromes, as we have maintained in a recent article on the Laurence-Moon-Biedl syndrome.[39]

39. Warkany, J.; Frauenberger, G. S., and Mitchell, A. G.: Heredofamilial Deviations: I. The Laurence-Moon-Biedl Syndrome, Am. J. Dis. Child. **53**:455-470 (Feb.) 1937.

Endocrine deviations from the normal, whether functional or morphologic, may be due to heredity. In order to determine whether or not associated defects have a causal relationship to one another, a thorough investigation of the patient's family history should be made. If two causally independent defects are found in one person, it often happens that these defects occur separately in other members of the family.[1a] If, for instance, goiter and a myopathy are found in one person, the observer may consider the muscular deficiency as subordinated to the thyroid deficiency. But if he takes pains to examine the family, he may find one member affected with myopathy but showing no goiter and another with goiter but no myopathy (fig. 6). This will immediately suggest that the myopathy is not due to dysfunction of the thyroid gland but is in reality a separate hereditary defect. This method of family investigation, although obviously helpful in many ways, is not employed sufficiently in investigation of etiologic factors.

CONCLUSIONS

Great care must be exercised in determining whether all defects and symptoms found in a patient with endocrine disturbance are necessarily causally related to it. Some of them certainly are not but represent, rather, associated hereditary or developmental defects. It is therefore not surprising that a hormone administered to different patients showing endocrine disturbances should give widely different results or have no effect at all on certain associated symptoms.

It should be emphasized that endocrinology has now reached a dangerous stage. A few years ago there were available only a few physiologically and pharmacologically active preparations of endocrine glands, such as thyroid extract, epinephrine and pitressin. Most of the other so-called endocrine preparations were either inert or largely so. Now there is an increasing number of products which affect the body; yet little is known of their quantitative effects and their unwanted by-effects, and too little also of their purity and "singleness," if one may use such a term. This confusion must not be increased by the attempt to treat with endocrine products conditions which are not caused by endocrine disturbance.

CARDIAC COMPLICATIONS OF ACUTE HEMORRHAGIC NEPHRITIS

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The observation, four years ago, of a patient with acute hemorrhagic nephritis in whom the predominating clinical manifestations were those of cardiac failure has led us to a more careful study of the status of the heart in patients with this illness. Since then, from October 1932 to October 1936, in a total of fifty-five patients with acute hemorrhagic nephritis admitted to the Children's Hospital of Philadelphia, we have observed fourteen children with varying degrees of cardiac involvement during the acute stage of their illness. Further analysis of the cases of these fifty-five patients revealed rather unexpectedly that cardiac involvement was the most frequent accompanying complication of acute hemorrhagic nephritis (table 1).

As far back as 1879 Goodhart [1] demonstrated cardiac dilatation in cases of postscarlatinal nephritis. More recently Guthrie [2] found cardiac hypertrophy at autopsy in seven of eight cases in which the blood pressure had been elevated during the course of the nephritis. Volhard [3] emphasized the significance of involvement of the heart during acute hemorrhagic nephritis and stated that

> almost every case that dies in the acute stage of the disease, dies of cardiac insufficiency through over dilatation. . . . This is very clearly recognized at necropsy.

There have also been some clinical studies of the status of the heart during acute nephritis (Levy,[4] Marcolongo [5]), but in the pediatric liter-

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From the Department of Pediatrics, School of Medicine, University of Pennsylvania, and the Children's Hospital of Philadelphia.

1. Goodhart, J. F.: Acute Dilatation of the Heart as a Cause of Death in Scarlatinal Dropsy, Guy's Hosp. Rep. **24**:153, 1879.

2. Guthrie, Katherine J.: Study of Pathology of Nephritis in Infancy and Childhood, J. Path. & Bact. **42**:565, 1936.

3. Volhard, F., in Berglund, H., and Medes, G.: Kidney in Health and Disease, Philadelphia, Lea & Febiger, 1935.

4. Levy, I. Jesse: The Cardiac Response in Acute Diffuse Glomerular Nephritis, Am. Heart J. **5**:277, 1930.

5. Marcolongo, F.: Il cuore nella glomerulonefrite acuta diffusa, Arch. per. le sc. med. **59**:975 and 1025, 1935.

ature the significance of cardiac damage has not been adequately emphasized.

A summary of the clinical course in each of our cases in which cardiac damage was encountered follows:

REPORT OF CASES

CASE 1.—J. Z., a 2 year old white girl with acute hemorrhagic nephritis, was admitted to the Children's Hospital of Philadelphia on Nov. 25, 1935, and died the following day. One week before she was admitted edema of the eyelids developed. The following day she became drowsy and refused food. The next day she began to vomit and it was noticed that her urine was scanty and bloody. Two days before her admission the edema was marked, she was noticeably ill and a cough had developed.

When she was admitted her temperature was 102 F. and her blood pressure 130 systolic and 90 diastolic. She was acutely ill and extremely edematous and had signs of cardiac failure.

TABLE 1.—*Cases of Acute Hemorrhagic Nephritis*

		Number
I. No complications		36
II. Complications		19
(a) Uremia (renal failure)	2*	
(b) Hypertensive encephalopathy	5*	
(c) Cardiac damage	14*	
Total		55

* One patient during the course of his illness exhibited all of these complications in the following order: renal failure, cardiac failure, hypertensive encephalopathy.

Treatment.—1. Magnesium sulfate was given both intramuscularly and by mouth in an attempt to relieve the hypertension. 2. Digitalis was given, but the child died before the complete digitalizing dose had been administered.

Course.—The child died with all the classic signs of acute cardiac failure. She was mentally clear during the entire time before death; in fact, a few hours before death she was standing in bed and asking to go home.

CASE 2.—M. A., a 5 year old white girl with acute hemorrhagic nephritis, was admitted to the hospital on March 6, 1934, and died March 15. Nephritis had developed during the course of otitis media. The urea nitrogen content of the blood was 122 mg. per hundred cubic centimeters. While this child was extremely toxic because of the nephritis, her death was sudden and was due to acute cardiac failure.

CASE 3.—M. S., a 5 year old white girl, was admitted to the hospital Feb. 18, 1936, with a history of impetigo of three weeks' duration. Three days before admission she became acutely ill with fever and then became edematous. Her urine was typical of acute hemorrhagic nephritis; her blood pressure was elevated (135 systolic and 85 diastolic), and she had signs of cardiac failure. The urea nitrogen content of the blood was 23 mg. per hundred cubic centimeters.

Treatment.—1. Magnesium sulfate was given immediately intramuscularly and was given orally and rectally throughout the duration of her hypertension. 2. Digitalization was carried out by the rapid method as soon as the child was

admitted.[6] 3. Morphine was given in appropriate doses for sedation. 4. Fluids were allowed as requested by the patient. For the first four days this child took approximately 24 ounces (720 cc.) daily. 5. The cutaneous lesions were treated with a 1 per cent aqueous solution of methylrosaniline after the crusts were removed.

Course.—The patient responded dramatically to this therapy. The day after her admission the blood pressure was down to 105 systolic and 70 diastolic. There was good elimination of urine, the edema decreased and the patient seemed greatly improved. She was no longer toxic and was breathing more easily. An electrocardiogram taken ten days after her admission was normal. Teleroentgenograms taken at this time showed a marked decrease in the size of the heart. The child continued to improve and on discharge, seven weeks later, she was asymptomatic, the urine was normal (Addis count normal) and there were no residual cardiac abnormalities. However, the sedimentation rate was still somewhat accelerated (20 mm., Cutler method).

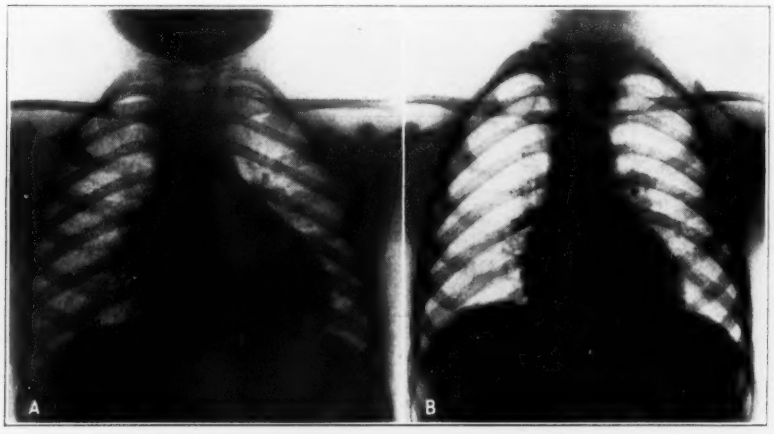

Fig. 1 (case 3).—*A*, teleroentgenogram taken on the day of admission to the hospital, showing cardiac enlargement. Transverse diameter of chest, 16.8 cm.; transverse diameter of heart, 10.2 cm. *B*, teleroentgenogram taken ten days after admission, when all cardiac symptoms had disappeared, showing marked reduction in the size of the heart.

CASE 4.—B. C., a 5 year old Negro girl, was admitted to the hospital on Dec. 8, 1935. Her illness began three weeks before admission, with fever and a rash. She had been exposed to scarlet fever. One week before admission she became edematous and her urine was scanty and bloody. The day before her admission her respirations were difficult and rapid. On admission she was desperately ill and in a state of collapse, with a rectal temperature of 96 F. and a blood pressure of 145 systolic and 110 diastolic. Moderate generalized edema and ascites were present. There was a residual infection of the upper respiratory tract, and her palms and soles were desquamating. She had moderately severe secon-

6. Digitalis given by the rapid technic was administered hypodermically as a fat-free tincture, in doses equivalent to 45 mg. of powdered whole leaf per kilogram of body weight. The total amount was given in a period of twelve hours.

dary anemia, and the urea nitrogen content of the blood was slightly elevated (44 mg. per hundred cubic centimeters). Her urine was typical of acute hemorrhagic nephritis. This patient exhibited the classic signs of acute cardiac failure.

Treatment.—After the application of external heat for shock, to which the child responded favorably, treatment was instituted as follows: 1. Magnesium sulfate was given intramuscularly, immediately and at intervals during the duration of her hypertension. 2. Digitalization was carried out by the rapid technic. 3. Morphine was given in appropriate doses for sedation. 4. The patient was placed in an oxygen tent, and phlebotomy was performed (150 cc.) in an attempt to relieve the load on the heart. 5. Fluids were restricted, being given in small amounts and only at the child's request.

Course.—After this therapy the child improved rapidly, with a fall in blood pressure, loss of edema, and disappearance of cardiac symptoms. The urea nitrogen content of the blood was normal eight days after her admission, and her urine

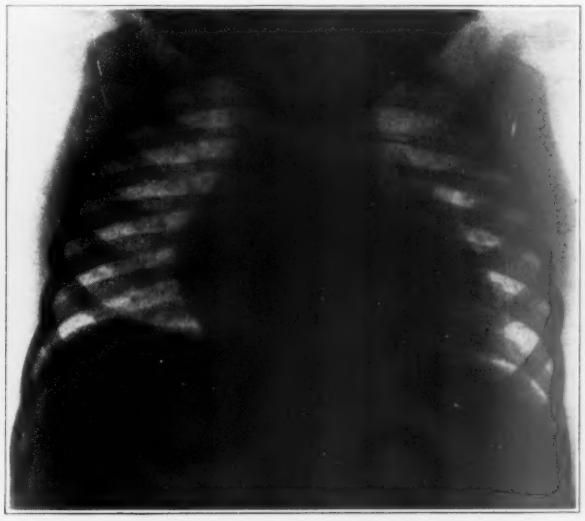

Fig. 2 (case 5).—*A*, teleroentgenogram taken three days after admission to the hospital, while the cardiac symptoms were still present, showing cardiac enlargement. Transverse diameter of chest, 15 cm.; transverse diameter of heart, 9.9 cm.

slowly cleared, but she still had an increased Addis count on her discharge, three months after her admission. Her sedimentation rate was rapid on her admission and at her discharge (30 mm.).

Case 5.—W. W., a 2 year old Negro boy, was admitted to the hospital Jan. 15, 1935, and discharged February 28. He had been under treatment with acetarsone for congenital syphilis. Two weeks before admission the child ate two tablets of acetarsone (four times his calculated daily dose). A few days later an acute infection of the upper respiratory tract developed, and after several days he began to pass bloody urine. No other symptoms were noted. On admission this boy had a normal temperature and a moderately elevated blood pressure (110 systolic and 82 diastolic). Although he did not appear extremely toxic, the examining physician was impressed by his obvious dyspnea. There were some puffiness of the eyelids and a moderate degree of pretibial edema. Signs of an infection

of the upper respiratory tract were present, and there were scattered coarse râles in both lungs. Signs of acute cardiac failure were present.

Treatment.—1. One ounce (28 cc.) of a 50 per cent solution of magnesium sulfate was given orally every four hours. 2. The patient was given fluids as he asked for them and took approximately 1,000 cc. daily.

Course.—Within five days after admission the patient had lost his edema and his signs of cardiac failure had disappeared. By the tenth day his blood pressure had returned to a normal level (95 systolic and 65 diastolic). The urine cleared in one week, and on physical examination before his discharge his heart was of normal size.

CASE 6.—N. B., an 8 year old white girl, was admitted to the hospital Nov. 20, 1935, and discharged Feb. 12, 1936. One week before admission she had an acute infection of the upper respiratory tract, becoming acutely ill, with fever, chills and vomiting. She also became edematous, and her breathing was rapid and deep. On

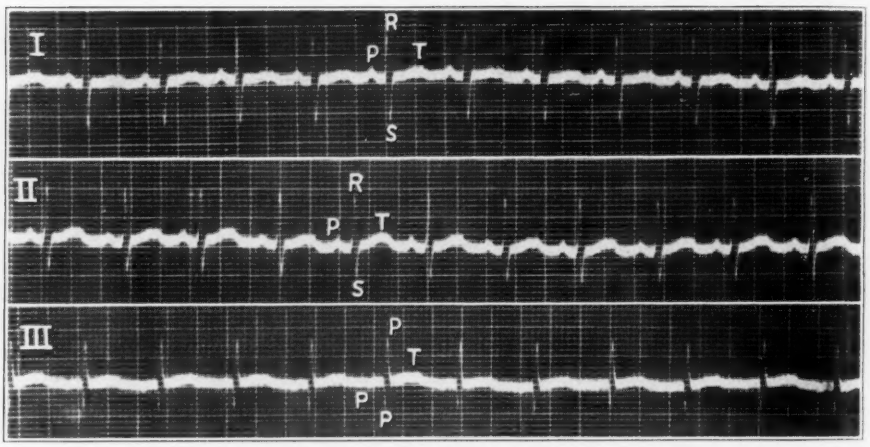

Fig. 3 (case 5).—Electrocardiogram, taken at the same time as the teleroentgenogram, shows slight slurring of the Q R S complex in leads II and III and a diphasic complex in leads I and III. The T wave is low and notched in lead I. This was interpreted by the cardiologist as demonstrating functional depression of the myocardium.

admission the child was obviously critically ill. She was semicomatose, was breathing deeply and rapidly and coughed occasionally. Her temperature was 104 F. Generalized edema was present. Signs of acute pharyngitis were found. Her urine was scanty and characteristic of acute hemorrhagic nephritis. Examination of the blood showed moderate secondary anemia, 32 mg. of urea nitrogen per hundred cubic centimeters of blood and acidosis (carbon dioxide-combining power 43 volumes per cent). The blood pressure was elevated, and the child exhibited signs of cardiac failure.

Treatment.—1. A 50 per cent solution of magnesium sulfate was given orally in doses of 1 ounce. 2. An attempt was made to force fluids because of her toxic condition. However, she took but 1,200 cc. daily. 3. Two days after admission she was digitalized by the rapid method.

Course.—After digitalization there was striking improvement. This semicomatose girl became alert, and the edema began to disappear. It had almost entirely disappeared two days after digitalization. The heart rate was normal one week afterward. The blood pressure slowly sank to a normal level and three weeks after her admission was 100 systolic and 60 diastolic, where it stayed until her discharge. When she was discharged the urine and heart were normal.

CASE 7.—D. W., an 8 year old Negro girl, was admitted to the hospital on Dec. 30, 1934. One month before her admission scarlet fever developed, and she was kept at a hospital for patients with contagious diseases for three weeks. The day after her discharge from that hospital it was noted that she had some edema of the face and extremities. The following day she vomited and had dyspnea on exertion. The dyspnea increased in severity and was associated with coughing. Three days before admission she had a series of convulsions; for the next two days her condition remained unchanged except that there were no further convulsions. On admission the child seemed acutely ill and was breathing with difficulty. Her temperature was normal, her pulse rate 120 and her blood pressure 164 systolic and 108 diastolic. Generalized edema and evidence of acute cardiac failure were present.

The urine had a sediment typical of hemorrhagic nephritis. The blood showed an elevated urea nitrogen content (67 mg. per hundred cubic centimeters) and moderately severe anemia. The rate of erythrocyte sedimentation was rapid.

The impression was that this child had acute hemorrhagic nephritis following scarlet fever. The convulsions occurring before admission indicated hypertensive encephalopathy.

Treatment.—1. Magnesium sulfate was given intramuscularly, by mouth and by retention enema. 2. Digitalization was carried out by the rapid method. 3. Sedation was obtained by suitable doses of phenobarbital. 4. Fluids were permitted as desired by the patient.

Course.—This child's general improvement was rapid. She lost 11 pounds (5 Kg.) of edematous fluid in a week, losing 5 pounds (2.3 Kg.) during the first three days. Her dyspnea and orthopnea disappeared with digitalization. Her blood pressure slowly fell to a normal level. There was marked reduction in the size of the heart as shown by comparative roentgenograms, and on her discharge from the hospital, three months later, the heart was almost normal in size. The electrocardiogram taken at the time of her discharge showed some myocardial damage. An apical murmur had completely disappeared. While the urea nitrogen of the blood fell to a normal level within ten days, after three months her urine still showed an abnormal number of formed urinary elements and her sedimentation rate was still rapid (28 mm.).

CASE 8.—J. McC., a 5 year old white boy, was admitted to the hospital Nov. 26, 1934, and discharged Feb. 13, 1935. Two days before his admission edema of the face developed, and the following day the urine was bloody and scanty. The day before admission he vomited. While there was no history of definite infection of the respiratory tract, it was stated that he wet his feet and became chilled two weeks before admission.

On his admission the temperature was 101 F., the pulse rate 120 and the respiratory rate 35 per minute. The patient did not seem acutely ill but was apathetic. Generalized edema and signs of infection of the upper respiratory tract were observed. The lungs were clear. Except muffled heart sounds, no cardiac abnormalities were noted. The blood pressure was 125 systolic and 85 diastolic. The liver was not enlarged. The urine showed elements encountered in hemor-

rhagic nephritis, and the urea nitrogen content of the blood was elevated (70 mg. per hundred cubic centimeters). The sedimentation rate of the blood was rapid (30 mm., Cutler method).

An attempt was made to force fluids by mouth, since there was no marked hypertension and the heart seemed to be in fairly good condition. The patient took 1,500 cc. of fluid daily. For the first two days marked oliguria was present, the patient voiding 120 cc. daily. Two days after his admission the blood pressure had risen to 145 systolic and 124 diastolic and evidences of circulatory embarrassment appeared, viz., the skin became cold and mottled, the heart tones became poor, a gallop rhythm developed, the liver enlarged and signs of congestion of the bases

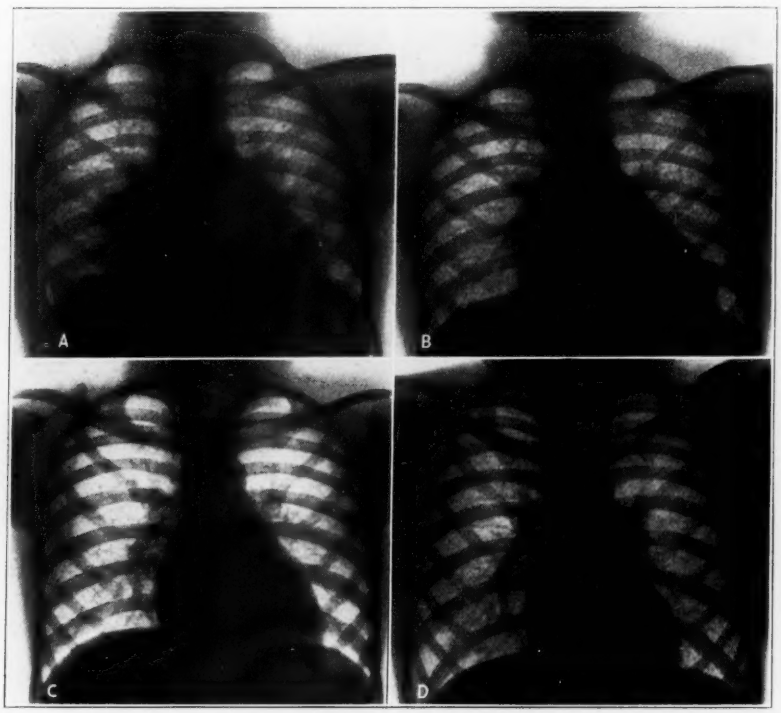

Fig. 4 (case 7).—*A*, teleroentgenogram taken three days after admission to the hospital, on the tenth day of illness, when the cardiac symptoms were beginning to regress, shows marked cardiac enlargement. *B*, *C* and *D* show progressive decrease in the size of the heart until normal limits are attained. The dates on the films show that the decrease occurred principally during the first three weeks.

of both lungs were detected. A teleroentgenogram taken at this time showed enlargement of the heart and passive congestion of both lungs. (In retrospect, we are inclined to believe that the forcing of fluids in this case may have helped to precipitate the cardiac phenomena.)

The only special therapy employed in this case was the frequent intramuscular administration of magnesium sulfate. The blood pressure slowly fell to a normal level, and the cardiac symptoms disappeared, the heart being normal at the time of discharge.

CASE 9.—J. F., a 5 year old white boy, was admitted to the hospital Oct. 29, 1932, and discharged December 16. One month before admission he had an acute infection of the upper respiratory tract. Nine days prior to admission he became febrile and his urine was bloody. A few days later he became edematous.

On admission the patient was acutely ill, with a pulse rate of 130 per minute, a temperature of 103 F. and an elevated blood pressure (150 systolic and 100 diastolic). Crusted impetiginous lesions were present on both legs. There was generalized edema, with moderate ascites. A profuse purulent discharge exuded

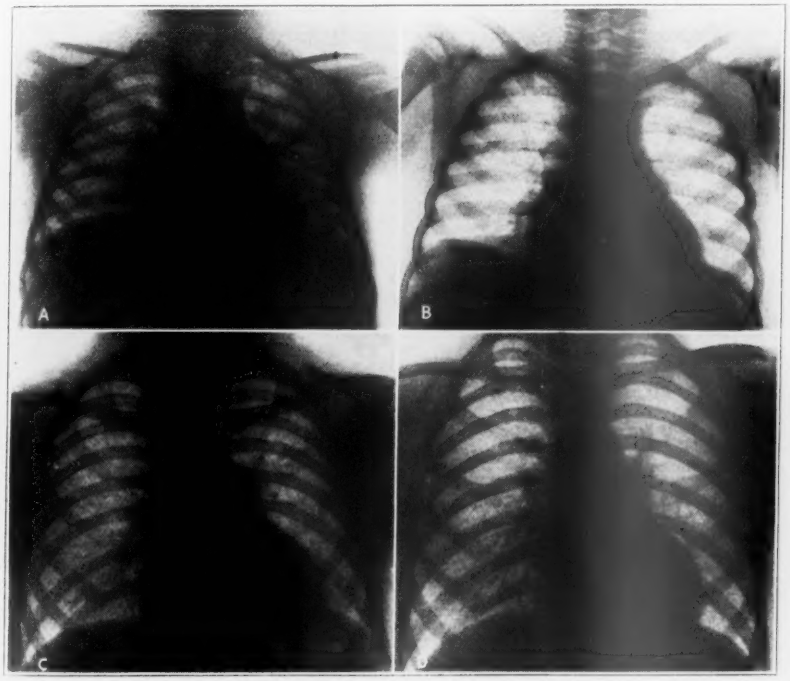

Fig. 5.—*A* (case 8), teleroentgenogram taken when cardiac symptoms were prominent, showing moderate cardiac enlargement. Transverse diameter of chest, 18.3 cm.; transverse diameter of heart, 10 cm.

B (case 10), teleroentgenogram taken one week after acute cardiac failure was noted, when the cardiac symptoms were subsiding, shows moderate cardiac enlargement. Transverse diameter of chest, 19 cm.; transverse diameter of heart, 11 cm.

C (case 12), teleroentgenogram taken a day after admission to the hospital, at the height of the cardiac symptoms, shows marked cardiac enlargement. Transverse diameter of chest, 20.5 cm.; transverse diameter of heart, 12 cm. *D* (case 12), was taken nine months after discharge from the hospital. Transverse diameter of chest, 20.5 cm.; transverse diameter of heart, 10.3 cm.

through small perforations of both ear drums. The heart was enlarged but seemed perfectly competent at this time.

The urine was typical of hemorrhagic nephritis, and the urea nitrogen content of the blood was elevated to 58 mg. per hundred cubic centimeters.

Treatment.—1. Two ounces (57 cc.) of a 50 per cent solution of magnesium sulfate was given orally every four hours. 2. The ear drums were incised to allow more adequate drainage. 3. Fluids were given the patient as he requested them, and for the first five days his average daily intake was 1,200 cc.

Course.—The day after admission the child seemed greatly improved. He was alert and comfortable, and there was a decrease in the edema. The blood pressure was still elevated (140 systolic and 105 diastolic). On the third day after his admission the oral administration of magnesium sulfate was discontinued because of the appearance of blood in the stools. He increased his fluid intake to 2,200 cc. daily. The following day it was noted that his blood pressure had risen to 180 systolic and 130 diastolic and that he had become more edematous. Later in the day it was found that his heart had increased considerably in size and that his liver had become tender. It was felt that the increased fluid intake and the discontinuance of magnesium sulfate were both of moment in contributing to the spurt in hypertension and to the beginning heart failure. Accordingly, magnesium sulfate was again given orally, and the fluid intake was restricted to 1,000 cc. Two days later the blood pressure had fallen to 120 systolic and 90 diastolic and the child had lost 8 pounds (3.6 Kg.) of edematous fluid. From this time the child steadily improved, and on discharge he seemed well clinically. The heart had returned to normal size, but the apical murmur was still present and there was still some hypertension, the blood pressure being 130 systolic and 100 diastolic. The urine still contained an occasional red blood cell.

CASE 10.—F. P., a 6 year old white boy was admitted to the hospital Aug. 17, 1936, and discharged October 11. One week before his admission his tonsils had been removed. Four days after his tonsillectomy he became chilled after playing under a fire hydrant. The following day he vomited several times, and edema of the face was noticed. During the three day period before his admission to the hospital he became increasingly edematous, his vomiting increased in intensity and frequency, he complained of fairly constant headache and he became drowsy. A progressive decrease in urinary output had begun with the onset of vomiting, and the urine was described as bloody. On admission the boy was stuporous and his breath had a uriniferous odor. The temperature was 99 F., the pulse rate 90, the respiratory rate 20 and the blood pressure normal (110 systolic and 80 diastolic). Moderate generalized edema was present. There was retinal hemorrhages in both eyegrounds. A greenish membrane covered both tonsillar fossae. The heart and lungs were normal. Roentgenographic examination of the sinuses revealed that the ethmoid cells were cloudy.

The urine contained large numbers of red cells and casts and a cloud of albumin. The urea nitrogen content of the blood was 85 mg. per hundred cubic centimeters and the rate of sedimentation of the blood was rapid (26 mm.).

Treatment.—Because of the history of extreme oliguria and because of the profound intoxication in the absence of hypertension, the following therapy was instituted: 1. Fluids were forced parenterally, 1,500 cc. being given daily. 2. Magnesium sulfate was given orally as a prophylactic measure against vascular spasm.

Course.—The day after admission the child was alert and bright, but because he had voided only a few ounces he was much more edematous. His oliguria persisted for a week, the urinary output not exceeding 100 cc. on any day. At the end of this seven day period his edema was extreme: The eyes were swollen shut, the abdomen was distended with a large collection of fluid, the scrotum and prepuce were water logged and the skin over the extremities was stretched to the

bursting point. However, the child was alert, requesting that the nurse or his mother read to him. During this entire period his blood pressure stayed within normal limits and his pulse rate was relatively slow (60 to 80 per minute). On the eighth day after his admission diuresis began and increased progressively. Four days after the onset of active diuresis, when he was voiding about 1,700 cc. daily, there was a sudden rise in blood pressure to 140 systolic and 105 diastolic and signs of cardiac failure became apparent. (The heart had been normal up to this time.) The pulse rate increased to 138 per minute, the heart tones became faint, a gallop rhythm appeared and there was extreme dyspnea, the respiratory rate being 72 per minute. At this time the following therapy was instituted: 1. Magnesium sulfate was now given intramuscularly. 8. Digitalization was carried out by the rapid method. 3. Fluids were restricted to 1,000 cc. daily.

The day after the institution of this therapy the condition of the heart began to improve: The heart tones were much better, and the signs of decompensation disappeared. The systolic blood pressure, however, remained elevated for ten days; it then fell to a normal level. During this ten day period the diastolic pressure fluctuated with the magnesium therapy but nevertheless was definitely elevated.

The patient's blood pressure remained at normal levels for nine days; magnesium sulfate therapy was then discontinued. The following day his blood pressure rose sharply to 182 systolic and 120 diastolic, symptoms of hypertensive encephalopathy developed and there was a renewal of cardiac embarrassment. Magnesium sulfate therapy was again started, large doses of sedative were given and 100 cc. of blood was removed by venesection. Improvement was rapid, the encephalopathic symptoms disappearing with the fall in blood pressure and the cardiac symptoms slowly clearing. At the time of his discharge, two weeks after this episode, there was still some cardiac hypertrophy. Nine months after his discharge the heart was still enlarged. This patient now presents evidence of chronic hemorrhagic nephritis.

Case 11.—E. U., a 5 year old white boy, was admitted to the hospital Aug. 19, 1934, and discharged October 25. Six days before admission the child complained of malaise and became drowsy. The next day he vomited several times. Although the vomiting was not repeated, he became increasingly ill, and on the day before his admission it was noted that his face and legs had become edematous and that his urine was bloody. About twelve hours prior to admission he began to cough, and dyspnea and orthopnea developed. There was no previous history of any infection of the respiratory tract.

On examination the temperature was normal, the pulse rate 115 per minute, the respiratory rate 50 per minute and the blood pressure 156 systolic and 110 diastolic. He was moderately dyspneic and orthopnic and had generalized pitting edema. Signs of an infection of the upper respiratory tract (pansinusitis) were present. Râles were audible throughout both pulmonary fields, and there were signs of acute cardiac failure.

The urine was typical of hemorrhagic nephritis, and the urea nitrogen content of the blood was 54 mg. per hundred cubic centimeters.

Treatment.—1. Magnesium sulfate was administered intramuscularly to relieve the vasospasm. 2. Digitalis was administered hypodermically by the rapid method. 3. Fluids were given as the child requested them. This child took 1,500 cc. daily. (At this time the importance of restriction of fluids in cases of nephritis with heart failure had not impressed itself on us.)

Course.—The day after the institution of the treatment the patient was more comfortable and less dyspneic. On the third day after his admission the blood

pressure was down to a normal level (114 systolic and 74 diastolic). However, it rose the following day to 154 systolic and 110 diastolic. It is interesting to note that the intramuscular injection of magnesium sulfate had been discontinued prior to this rise. By August 25, six days after the patient's admission, the blood pressure was again normal (108 systolic and 74 diastolic), and it remained normal until his discharge. By the end of the first week after his admission the edema had completely disappeared and he had lost 7 pounds (3.2 Kg.) of weight. Evidences of cardiac decompensation had disappeared by this time, and the urea nitrogen content of the blood was approximately normal.

CASE 12.—L. M., a 10 year old boy, was admitted to the hospital on April 14, 1936, and discharged on May 21. A week before his admission an acute infection of the upper respiratory tract developed. The following day his urine became bloody and he became edematous. The next day he was drowsy and vomited several times. The drowsiness and vomiting continued. The day before admission he had generalized convulsions.

He was admitted with a convulsion, which subsided as he sank into a stupor. He was pale and edematous. His temperature was 101 F., his pulse rate 130 per minute and his blood pressure 180 systolic and 126 diastolic. There were signs of an acute infection of the upper respiratory tract and signs of cardiac failure.

The urine contained albumin, many red blood cells and many casts. The urea nitrogen content of the blood was 28.5 mg. per hundred cubic centimeters. The rate of sedimentation of the blood was rapid (30 mm.).

Treatment.—1. Magnesium sulfate was given intramuscularly and by mouth. 2. Morphine was given. 3. Rapid digitalization was employed. 4. Fluids were allowed as desired. The child took 1,400 cc. daily for the first few days.

Course.—The day following the onset of treatment the child's condition was improved. He was alert, and the blood pressure had fallen to 150 systolic and 102 diastolic. The edema decreased. The blood pressure continued to fall and after one week was within normal limits, where it remained. When he was discharged his heart was almost normal in size and his urine was practically normal. An electrocardiogram taken ten months after his discharge showed some residual myocardial damage.

CASE 13.—J. E., a 4 year old white boy, was admitted to the hospital on Aug. 7, 1935. Three weeks before admission he had acute pharyngitis; subsequently he became edematous. His urine became scanty and bloody. Two days before admission he became more acutely ill, his edema increased and he became drowsy.

On examination he was afebrile, pale and acutely ill. Generalized edema and ascites were present. There was no evidence of infection of the upper respiratory tract. The pulse was rapid, the rate being 100 per minute, and the blood pressure was elevated (150 systolic and 110 diastolic). Evidences of myocardial damage were present, but the heart was competent.

The urine was typical of hemorrhagic nephritis. The urea nitrogen content of the blood was elevated (46 mg. per hundred cubic centimeters), and the carbon dioxide combining power was 38 volumes per cent. The urinary output was decreased. Anemia was present.

Treatment.—1. Magnesium sulfate was given by mouth. 2. Fluids were allowed as desired.

Course.—The drowsiness rapidly disappeared, and the blood pressure slowly fell to a normal level. The boy was taken home six weeks after admission, before he was entirely well. His urine still contained albumin, many red blood cells and many casts. His heart was normal.

CASE 14.—V. H., a 7 year old Negro girl, was admitted to the hospital Sept. 30, 1935, and discharged November 22. A week before her admission an acute infection of the respiratory tract and cervical adenitis developed. The day before her admission there was slight pain in the upper part of the abdomen. There were no other complaints.

On examination the child did not seem acutely ill. The temperature was 101 F. The pulse rate and the respiratory rate were in keeping with this temperature. There was no edema. Signs of residual infection of the upper respiratory tract were present. A few coarse râles were scattered throughout the bases of both lungs. The blood pressure was 135 systolic and 98 diastolic. The heart was enlarged but the sounds and the rhythm were normal. A teleroentgenogram taken three weeks later showed a slight increase in the width of the heart in both directions.

The urine contained albumin, red blood cells, casts and white blood cells. The urea nitrogen content of the blood on the patient's admission was normal (19 mg. per hundred cubic centimeters).

Treatment.—1. Magnesium sulfate was given orally. 2. Fluids were given as desired by the child.

Course.—The child's weight remained constant; there were no evidences of edema. The blood pressure fell rapidly to normal within four days. The urine cleared slowly, being normal when the patient was discharged. The status of the heart on her discharge was not recorded. However, examination fifteen months later showed the heart to be normal.

We have presented our cases in the order of decreasing degrees of cardiac involvement. Thus in cases 1 and 2 the children died of acute heart failure; in cases 3, 4, 5, 6 and 7 they had active heart failure at the time of admission to the hospital; in cases 8, 9 and 10 active heart failure developed while they were under observation in the hospital; in cases 11 and 12 they exhibited mild symptoms of heart failure, and in cases 13 and 14 they presented signs of myocardial damage, although no actual heart failure developed.

The clinical evidences of cardiac involvement and failure observed in our cases of acute hemorrhagic nephritis were:

1. Dyspnea, tachypnea and cough.

2. Cardiac enlargement, demonstrable both by physical examination and in teleroentgenograms.

3. Muffled heart tones.

4. Rapid heart rate. Volhard[7] stated that in the adult patient with uncomplicated acute hemorrhagic nephritis the pulse rate is slower than normal and that a rate of 80 per minute or more would suggest cardiac involvement. In our children we did not observe bradycardia except in one case (this child having no evidence of cardiac involvement). Furthermore, the instability of the pulse rate in children in health or in disease would make evaluation of this sign difficult.

7. Volhard, F., in von Bergmann, G., and Staehelin, R.: Handbuch der inneren Medizin, Berlin, Julius Springer, 1931, vol. 6, pt. 2.

5. Murmurs, usually a mitral systolic murmur. This murmur was often the last evidence of cardiac damage to disappear as the patient recovered.

6. Gallop rhythm. This was present in the patients with more advanced heart failure.

7. Enlargement and tenderness of the liver.

8. Engorgement of the venous system.

9. Pulmonary edema.

10. Peripheral edema. It was impossible to estimate how much of the edema in a given case was due to damage to the kidney itself and to what extent the heart failure was contributing. However, after digitalization of the nephritic patients with heart failure there was often a striking decrease in the amount of edema.

11. Electrocardiographic changes indicative of varying degrees of myocardial damage.

Table 2 lists the occurrence in our cases of the symptoms referable to cardiac involvement.

COMMENT

That there is involvement of the heart in acute hemorrhagic nephritis is not at all surprising. During the acute phase of the disease two factors are operative which may affect the heart adversely, viz., myocardial damage and increased peripheral vascular resistance (hypertension).

In regard to *myocardial damage*, it is possible that the same infective agent responsible for the acute nephritis damages the heart. The work of Longcope and his co-workers [8] showed that the hemolytic streptococcus is intimately associated with acute hemorrhagic nephritis. The occurrence of myocardial damage during the course of acute streptococcic infections appears to be fairly frequent. Thus, in fatal scarlet fever myocarditis is extremely common. In a study of autopsy material by Magladery and Billings [9] in Aschoff's laboratory, varying degrees of myocarditis were seen in twenty-nine of thirty-seven cases. Similarly,

8. Longcope, W. T.; O'Brien, D. P.; McGuire, J.; Hansen, O. C., and Denny, E. R.: Relationship of Acute Infections to Glomerular Nephritis, J. Clin. Investigation **5**:7, 1927. Winkenwerder, W. L.; McLeod, N., and Baker, M.: Infection and Hemorrhagic Nephritis, Arch. Int. Med. **56**:297 (Aug.) 1935. Longcope, W. T.: Studies of the Variations in the Antistreptolysin Titer of the Blood Serum from Patients with Hemorrhagic Nephritis, J. Clin. Investigation **15**:269, 1936.

9. Magladery, I. W., and Billings, F. T.: Ueber die Unterschiede in der Stärke der Scharlachmyocarditis bei den einzelnen Epidemien, Beitr. z. path. Anat. u. z. allg. Path. **97**:205, 1936.

TABLE 2.—*Symptoms Referable to Cardiac Involvement in Cases of Acute Hemorrhagic Nephritis*

Patient	Age	Blood Pressure on Admission	Blood Pressure on Discharge	Dyspnea	Cardiac Enlargement	Poor Heart Tones	Tachycardia	Murmur	Gallop Rhythm	Enlarged Liver	Engorgement of Veins of Neck	Pulmonary Edema	Peripheral Edema	E. C. G. Changes
J. Z.	2	130/ 90	Died	+	+	+	+	0	+	+	+	+	+	Not done
M. S.	5	130/ 85	105/ 70	+	+	+	+	Systolic apical	0	+	Not noted	+	+	Not done
B. C.	5	140/110	100/ 68	+	+	+	+	Systolic apical	+	+	+	+	+	+
W. W.	2	110/ 82	95/ 65	+	+	+	+	0	+	+	Not noted	+ (?)	+	+
N. B.	8	134/100	100/ 60	+	+	+	+	0	+	+	+	0	+	Not done
D. W.	8	164/108	105/ 80	+	+	+	+	Systolic apical	+	0	+	0	+	+
J. McC.	5	145/124	102/ 70	+	+	+	+	Systolic apical	+	+	+	+	+	Not done
J. F.	5	180/130	130/100	+	+	+	+	Systolic apical	0	+	Not noted	0	+	Not done
F. P.	6	150/110	112/ 72	+	+	+	+	Systolic apical	+	+	+	0	+	Not done
E. U.	5	156/110	105/ 65	+	+	+	+	Systolic apical	+	+	Not noted	+	+	+
L. M.	10	180/126	118/ 70	0	+	0	+	Systolic apical	0	0	0	+ (?)	+	+
J. E.	4	150/110	90/ 55	0	+	+	+	0	+ (?)	+	0	0	+	+
V. H.	7	135/ 98	110/ 60	+	+	0	+	0	0	0	0	0	..	Normal
M. A.	5	.....	.....	Cyanosis	No notes on record as to status of heart other than that patient died of acute heart failure									

Stoeber [10] observed microscopic evidences of myocarditis in sixteen of twenty-two fatal cases of scarlet fever. Brody and Smith [11] stated that myocardial lesions of varying severity were encountered in more than 90 per cent of the fatal cases of scarlet fever and related streptococcic infections.

The limited studies of autopsy material in cases of trench nephritis show that myocardial damage does occur but is not similar to that seen in scarlet fever. While the common myocardial lesion described in scarlet fever appears to be an inflammatory one, the reported changes in the myocardiums of patients dying of acute hemorrhagic nephritis during the war were degenerative. Franke [12] and Jungmann [13] recorded cases in which the cardiac muscle fibers showed a diffuse mottling with fine fat droplets and a loss of striations. However, microscopic changes in the heart have not been constantly observed in cases of acute hemorrhagic nephritis in which death was caused by myocardial failure.

If the renal lesion in acute hemorrhagic nephritis is anaphylactoid in character, it is possible that the cardiac involvement may be of similar etiology.

Furthermore, the retained metabolites may exert an adverse influence on the myocardium.

The second factor, *hypertension* (which is evidence of increased peripheral resistance brought about by vasospasm),[14] is the agent immediately responsible for the impairment of cardiac function. In our experience, hypertension has been present in all patients with acute hemorrhagic nephritis exhibiting signs of cardiac insufficiency. This is in keeping with Volhard's observations.[7] The usual response of the heart to an increase in peripheral resistance is dilatation of the left ventricle, with ultimate hypertrophy. In those cases in which the heart is primarily involved by the disease it is likely to fail under the added load of a sudden increase in peripheral resistance. *Whether or not heart failure results, therefore, is dependent on two factors, the extent of the myocardial damage and the degree of hypertension.*

Levy [4] found that hypertension was absent in some of his cases of heart failure during acute nephritis. From our observations it was

10. Stoeber, E.: Ueber Myokarditis bei Jugendlichen besonders Scharlachmyokarditis, Arch. f. Kinderh. **105**:193, 1935.

11. Brody, Henry, and Smith, Lawrence W.: The Visceral Pathology in Scarlet Fever and Related Streptococcus Infections, Am. J. Path. **12**:373, 1936.

12. Franke, Maryan: Beiträge zur Nephritisfrage. Ueber das Verhalten des Herzens und der grossen Gefässe bei akuten Nierenentzündungen, Deutsches Arch. f. klin. Med. **122**:428, 1917.

13. Jungmann, Paul: Ueber akute Nierenerkrankungen bei Kriegsteilnehmern, Ztschr. f. klin. Med. **84**:1, 1917.

14. Pickering, G. W.: Peripheral Resistance in Persistent Arterial Hypertension in Acute Nephritis, Clin. Sc. **2**:209, 1936.

noted that blood pressure values which were not considered abnormal at the first reading were actually elevated in comparison with values obtained after the patient was entirely well (table 2). Caution must be exercised in evaluating isolated readings of children's blood pressure. Furthermore, in the hypertensive child elevation of the diastolic pressure is of greater import and is a more constant finding than elevation of the systolic blood pressure. Volhard [7] stated: "In cases without appreciable rise of systolic pressure, especially in small children, an increased peripheral resistance may only be manifested by an increase in diastolic pressure."

A review of the fifty-five cases of nephritis in this series did not show any correlation between the severity of renal manifestations and the

TABLE 3.—*Subsequent Status of Heart in Patients Exhibiting Cardiac Involvement During Acute Hemorrhagic Nephritis*

Case No.	Patient	Condition on Discharge From Hospital	Condition on Reexamination
1	J. Z.	Died	
2	M. A.	Died	
3	M. S.	Heart normal	Heart normal one year later
4	B. C.	Heart normal	Heart normal fourteen months later
5	W. W.	Heart normal	Heart normal two years later
6	N. B.	Heart normal	Heart normal thirteen months later
7	D. W.	Moderate cardiac enlargement	Heart normal six months later
8	J. McC.	Heart normal	Heart normal two years later
9	J. F.	Heart normal size, apical murmur	
10	F. P.	Moderate cardiac enlargement	Mild cardiac enlargement nine months later
11	E. U.	Heart normal	Heart normal
12	L. M.	Slight enlargement	Heart normal ten months later except for some electrocardiographic evidence of myocardial damage
13	J. E.	Heart normal	Heart normal
14	V. H.	Heart normal	Heart normal

occurrence of cardiac complications. Thus the fourteen patients who had cardiac damage did not evidence a more severe degree of nephritis than did the patients without this complication. Furthermore, there was no appreciable difference in the duration or in the outcome of the nephritis itself in the two groups of cases.

Table 3 shows the status of the hearts of the fourteen patients with cardiac involvement after recovery from the acute phase of hemorrhagic nephritis. In only one of the patients was there any evidence of permanent cardiac damage, and this patient now gives evidence of chronic hemorrhagic nephritis.

It is of great interest and significance that the only deaths which occurred in the entire group of fifty-five nephritic patients were due to cardiac failure.

THERAPY

Volhard stated that every patient with acute hemorrhagic nephritis should be looked on as one in whom acute heart failure may develop. The high incidence of cardiac involvement in our group of patients brings us into entire accord with this point of view.

It is impossible to dissociate the treatment of the cardiac manifestations of acute hemorrhagic nephritis from the general management of the disease itself. A consideration of the interrelations of the various factors operative in a case of acute nephritis makes it obvious that heart failure is not an isolated phenomenon but is intimately related to other factors. Figure 6 graphically illustrates these interrelations.

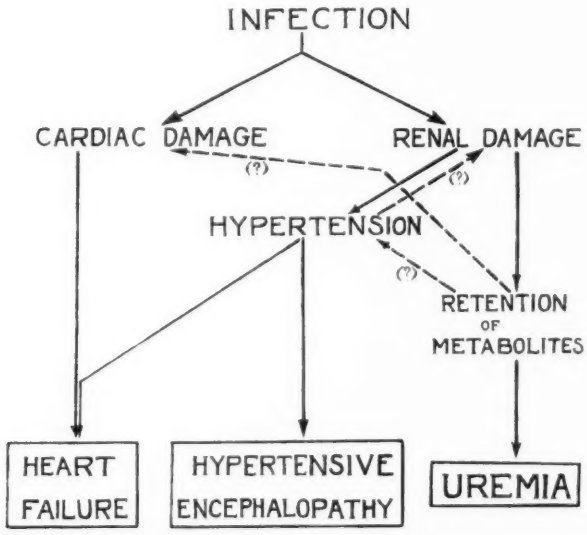

Fig. 6.—Diagram showing interrelations of the various factors operative in a case of acute nephritis.

In a given case, if the heart seems normal, if there is no marked elevation of the blood pressure and if the major disturbance is the retention of metabolites caused by decreased activity of the kidney, therapy might include the forcing of fluids in an attempt to dilute the toxins and produce diuresis. When severe acidosis is present, the administration of alkali (e. g., sodium lactate) should be considered.

Figure 7 depicts the course in such a case. This patient had anuria for five days. During the period of anuria fluids were given in large amounts. Despite the increasing edema, which is reflected in the weight curve, the intoxication was definitely lessened. It is possible that the concentration of retained metabolites (indicated by the curve of urea

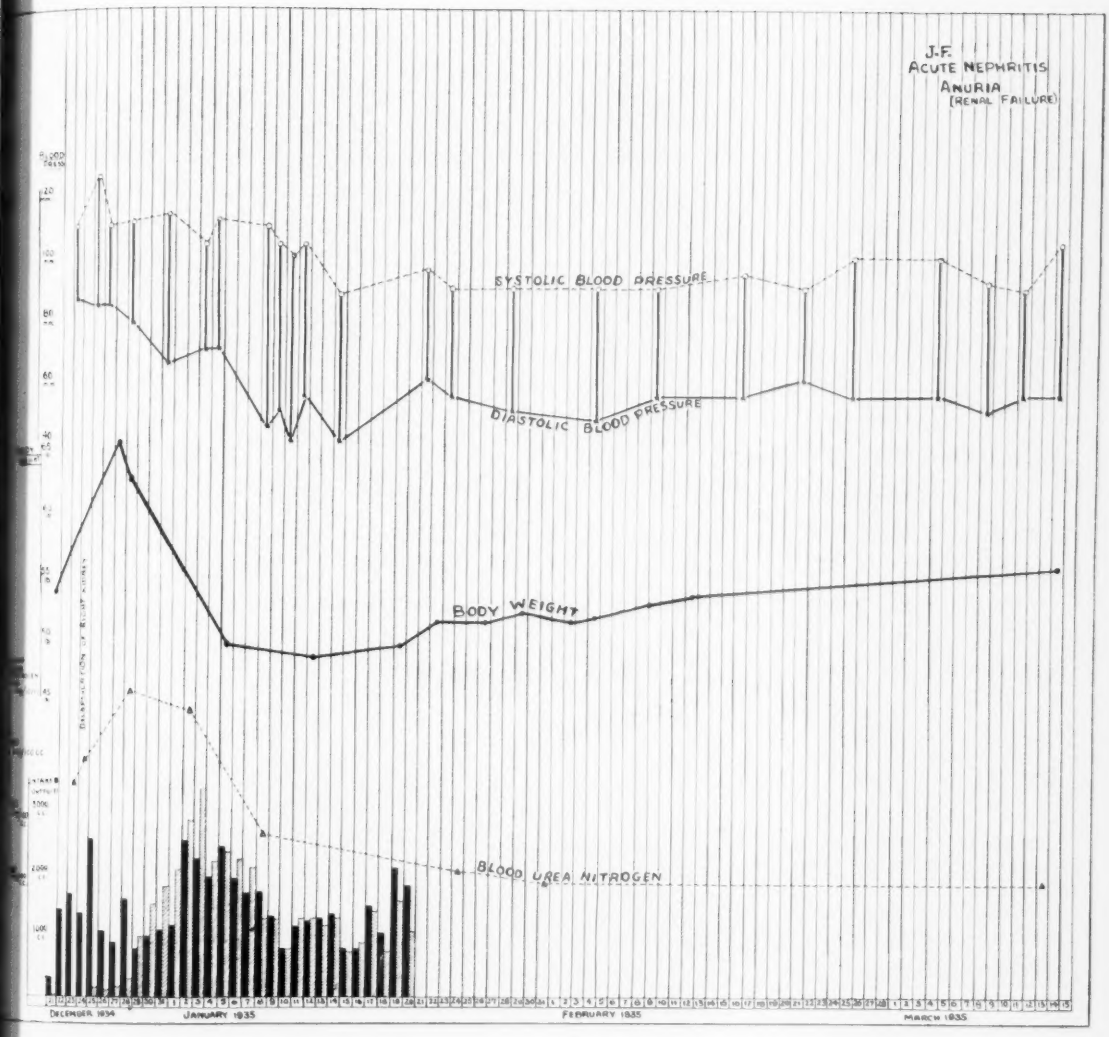

Fig. 7.—Chart of a case of acute nephritis with anuria but with apparently normal heart and blood pressure.

nitrogen) would have been greater if fluids had not been given. The reasons for the spontaneous onset of diuresis were not apparent.

Repeated readings of the blood pressure should be taken in these cases, for sudden rises may occur. If the blood pressure should rise or if there should occur any symptom or sign referable to myocardial damage, fluids should be restricted and further therapy, which will be described, should be instituted.

In cases of acute hemorrhagic nephritis in which *hypertension is present,* the control of the hypertension is important with reference to the encephalopathic syndrome, but it is of even more moment in the prevention of cardiac failure. The studies of Pickering [14] have furnished rather convincing evidence that the hypertension in this disease has its origin in increased vasospasm. It should be emphasized again that in those cases in which primary myocardial damage is present in conjunction with hypertension, heart failure may ensue. Consequently, therapy directed at relieving the heart of the added work resulting from vasospasm should be instituted immediately. To relieve vasospasm we have used magnesium sulfate.

Experimental work done in our laboratory [15] indicates that magnesium is capable of relieving vasospasm. In these experiments, prolonged hypertension was induced in rats by the injection of a vasospastic agent, ergotamine tartrate. Magnesium carbonate added to the diet prevented the hypertension, if given before the injections of ergotamine tartrate, and when given to animals after they were rendered hypertensive by this drug it brought the blood pressure back to within normal limits.

Observations made on a 7 year old boy with acute hemorrhagic nephritis and hypertension furnished additional evidence concerning the action of magnesium in reducing hypertension. The child was placed on a constant intake of fluid (30 cc. per hour), and the hourly output of urine was determined. After a period of observation, 90 cc. of a 50 per cent solution of sucrose was administered intravenously. This was followed by marked diuresis, but the blood pressure was not influenced and remained at its previously high level. Fourteen hours later a 50 per cent solution of magnesium sulfate was given intramuscularly (0.2 cc. per kilogram of body weight). After this there was a prompt drop in both systolic and diastolic blood pressure, with no accompanying diuresis. These events are graphically illustrated in figure 8.

These observations, we believe, show that magnesium sulfate reduces hypertension by releasing vascular spasm. Granted that both

15. Rubin, M. I., and Rapoport, M.: Action of Magnesium-Effect of Magnesium on Vascular Spasm, Am. J. Dis. Child. **52**:743 (Sept.) 1936; Effect of Magnesium on Vascular Spasm in Rats, Arch. Int. Med. **59**:714 (April) 1937.

the magnesium and the sulfate ions are diuretic agents, nevertheless the amount of diuresis produced with the amounts of magnesium sulfate given to our patients was insignificant. The beneficial effect of magnesium similarly administered to patients with hypertensive encephalopathy has been ascribed to the dehydrating action of magnesium sulfate. Certainly the results of the clinical experiment here recorded furnish no support to this point of view. It is our feeling, rather, that the beneficial effects of magnesium in cases of hypertensive encephalopathy are intimately related to the relief of vasospasm. Some observers

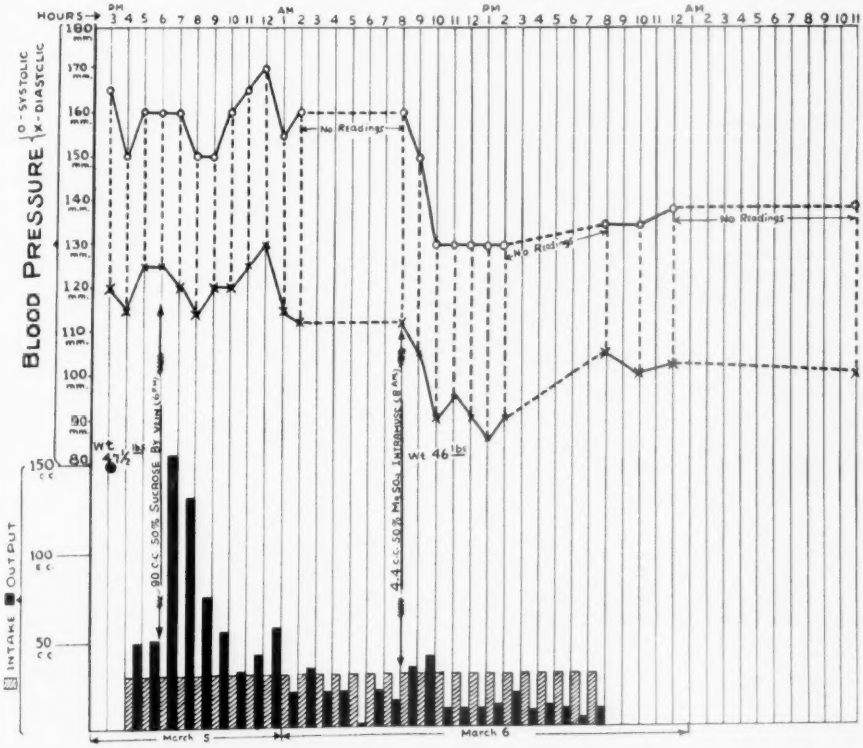

Fig. 8.—Chart of a case of acute hemorrhagic nephritis. This shows the effect of a hypertonic (50 per cent) solution of sucrose given intravenously and of a 50 per cent solution of magnesium sulfate given intramuscularly on the output of urine and on the blood pressure.

have expressed the belief that the underlying cause of hypertensive encephalopathy is vasospasm.[16]

In figure 9, which is a graphic representation of a case of hypertensive encephalopathy, the beneficial effects of magnesium sulfate in

16. McAlpine, D.: The Hypertensive Cerebral Attack, Quart. J. Med. **2**: 463, 1933.

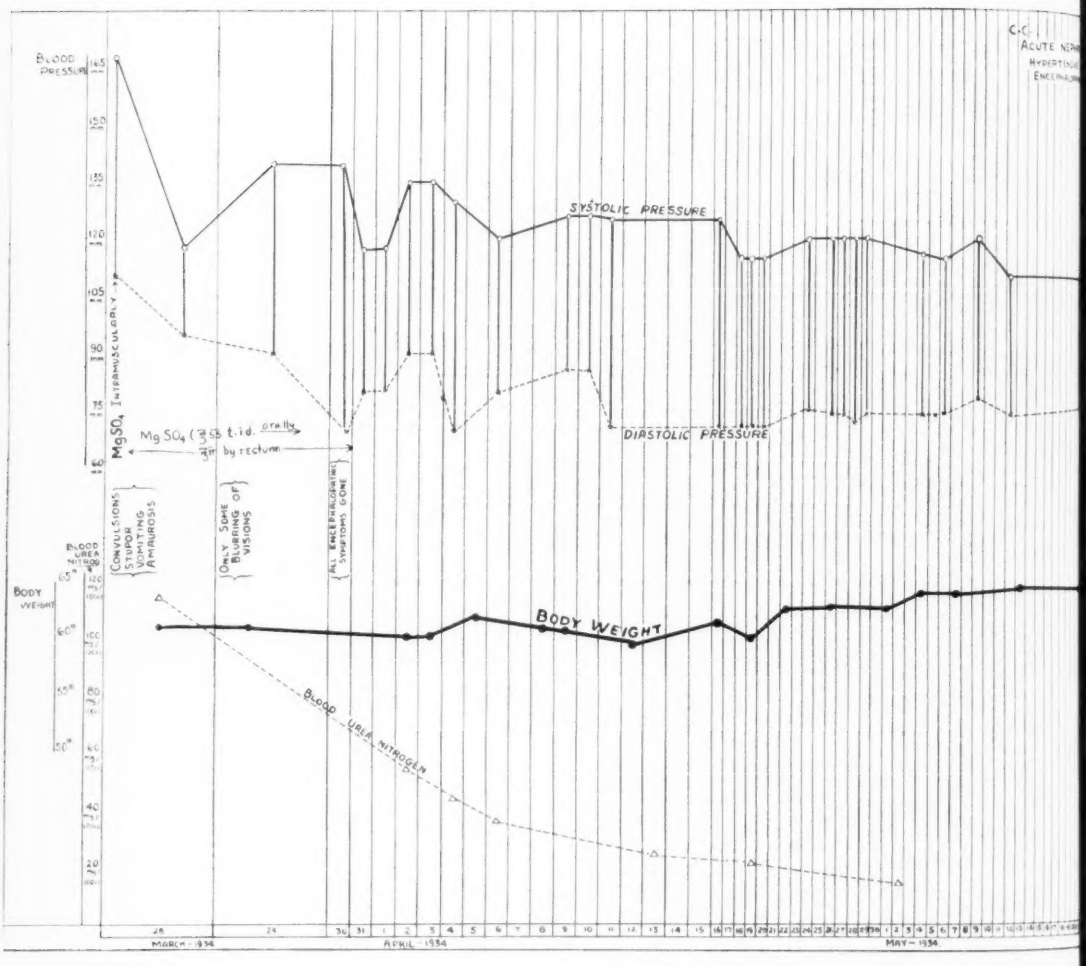

Fig. 9.—Chart of a case of acute nephritis with hypertensive encephalopathy, showing effects of magnesium sulfate.

relieving the symptoms and reducing the blood pressure are apparent. This relief occurred without dehydration of sufficient magnitude to influence the weight curve.

We have administered magnesium sulfate by intramuscular injection, using a dose of 0.2 cc. of a 50 per cent solution per kilogram of body weight. The effects of a single dose are usually prompt. The systolic and diastolic pressures begin to subside within an hour and remain down for several hours. The full dose may be repeated at four hour intervals. In some cases one calculated dose of magnesium sulfate may have no effect. In such instances we feel that it is safe to repeat the injections at shorter intervals. One caution must be observed in administering magnesium sulfate. In cases with marked renal impairment in which the urinary output is low and in which there is a marked retention of metabolites, it is possible that the accumulation of magnesium in the body may exert a narcotic effect, as was pointed out by Hirschfelder.[17] We have not encountered this ill effect of magnesium sulfate. However, should one suspect that coma or extreme drowsiness in a patient receiving magnesium sulfate was caused by the drug, one of the soluble calcium salts could be employed as an effective antidote.

It is our conviction that fluids should be restricted in cases of acute hemorrhagic nephritis with *hypertension,* for in the administration of liberal amounts of fluid there is danger of producing a further elevation of blood pressure and precipitating a cardiac catastrophe. Dorner[18] demonstrated that the ingestion of a large amount of fluid by the patient without nephritis resulted in a rise of blood pressure, which he attributed to the increased blood volume.

In any particular case, it is impossible to designate an absolute quantity of fluid which may be given with safety. It is our practice to offer fluids to the child as they are requested. While some of our patients have taken without apparent harm amounts of fluid which we now regard as excessive, we believe it is safer to limit the fluid intake of nephritic patients during the period of acute hypertension. At present we limit the fluid intake to an arbitrary level of from 750 to 1,000 cc. daily. Since the hypertension is usually of short duration, fluids are restricted only until the blood pressure has subsided to a level within relatively normal limits, after which fluids may be given in liberal amounts to further diuresis. In cases of acute nephritis without hyper-

17. Hirschfelder, A. D.: Clinical Manifestations of High and Low Plasma Magnesium: Dangers of Epsom Salt Purgation in Nephritis, J. A. M. A. **102:** 1138 (April 7) 1934.

18. Dorner, G.: Ueber Beziehungen zwischen Blutdruck und Wasserzufuhr bei Nephritiden, insonderheit bei der Feldnephritis, Deutsches Arch. f. klin. Med. **133:**21, 1920.

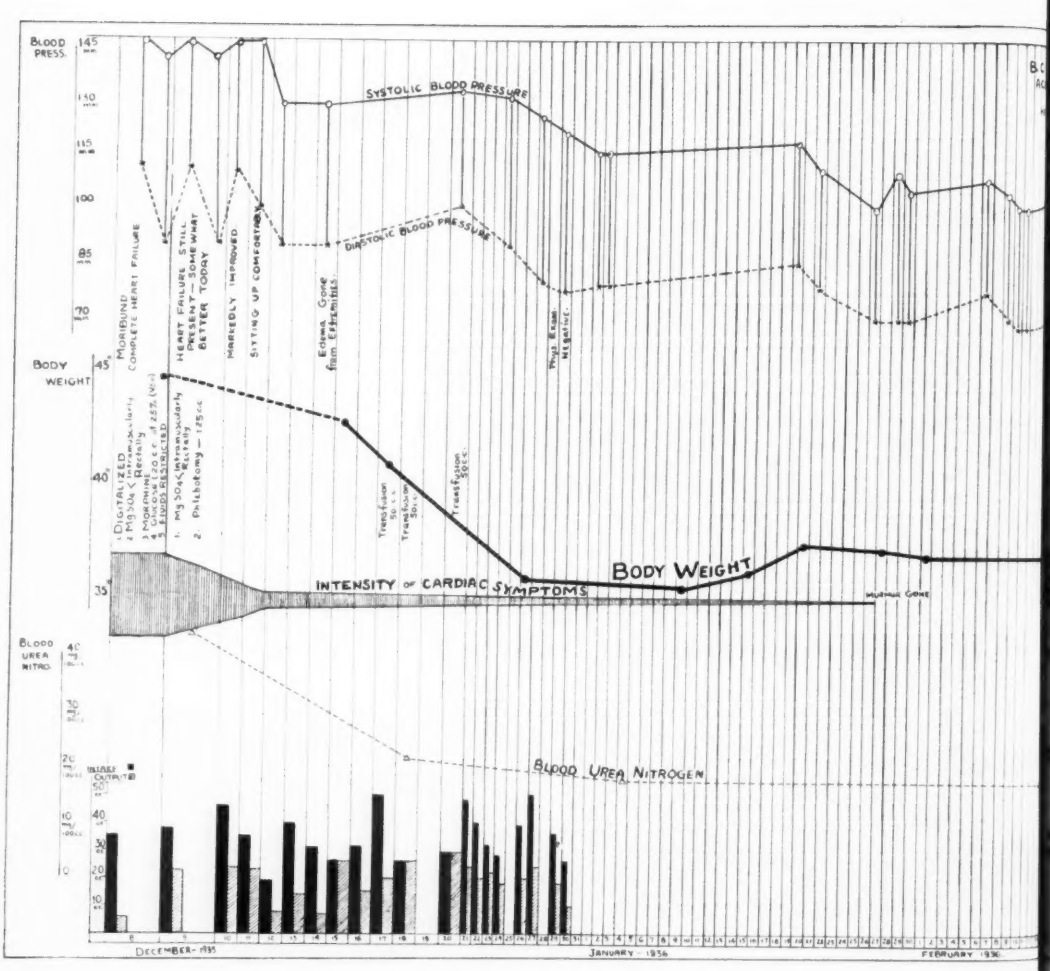

Fig. 10.—Chart of a case of acute nephritis with heart failure, showing effect of magnesium sulfate on the diastolic blood pressure.

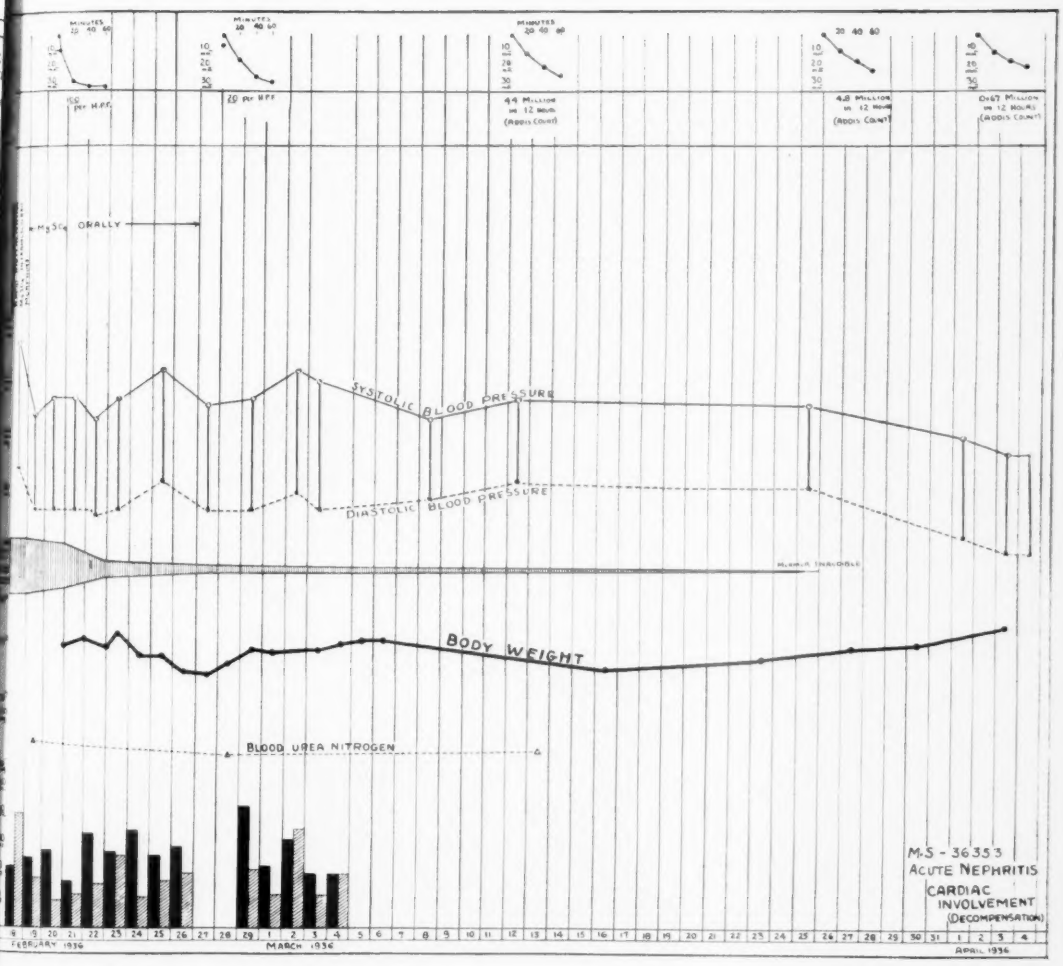

Fig. 11.—Chart of a case of acute nephritis with heart failure, showing rapid decrease of blood pressure and improvement of the heart with use of magnesium sulfate, digitalis and sedation.

tension and without cardiac involvement, fluids may be given in liberal amounts, as was stated previously.

In cases in which there was evidence of cardiac damage, supportive measures for the heart were instituted in addition to the use of magnesium sulfate and the limitation of fluid intake. Digitalis was administered by the rapid method to patients showing signs of cardiac failure; the dose was 45 mg. of powdered leaf per kilogram of body weight (usually given hypodermically as fat-free tincture in a period of twelve hours). After administration of the complete digitalizing dose we usually found it unnecessary to continue with a maintenance dose.

In cases in which there was cardiac involvement of any degree, sedation (morphine) was valuable. The administration of oxygen seemed to benefit patients with respiratory symptoms resulting from heart failure. Phlebotomy was done on two patients with more advanced cardiac failure. Although a hypertonic (50 per cent) solution of dextrose was given to several patients with cardiac failure for its supposedly beneficial action on the failing myocardium, we were unable to evaluate its effect.

Figures 10, 11 and 12 graphically depict the management of patients presenting cardiac failure during the course of acute hemorrhagic nephritis.

In figure 10 it is apparent that in this case the magnesium sulfate affected chiefly the diastolic pressure, which dropped sharply after each injection. It is possible that a larger dose of this salt would have exerted a greater effect on the systolic pressure than was obtained.

Figure 11 shows the rapid disappearance of cardiac failure after the combined use of magnesium sulfate, digitalis and sedation. The decrease in blood pressure paralleled the improvement in the cardiac symptoms.

Figure 12 illustrates the sequence of events in the case of F. P. (case 10). This patient was admitted to the hospital with renal failure (marked oliguria). During this period fluids were forced, and as a result of persistent oliguria the patient became extremely edematous. At the height of the edema there was a sharp rise in blood pressure associated with signs of cardiac failure which persisted over a long period. Concurrent with the slow fall in blood pressure, there was gradual improvement of the cardiac condition. After the cessation of magnesium sulfate therapy and the ingestion of a large amount of water, there was a steep rise in blood pressure which was soon followed by symptoms of hypertensive encephalopathy and aggravation of the condition of the heart.

SUMMARY

Fifty-five cases of acute hemorrhagic nephritis in children were studied. Severe myocardial damage was encountered in fourteen of the

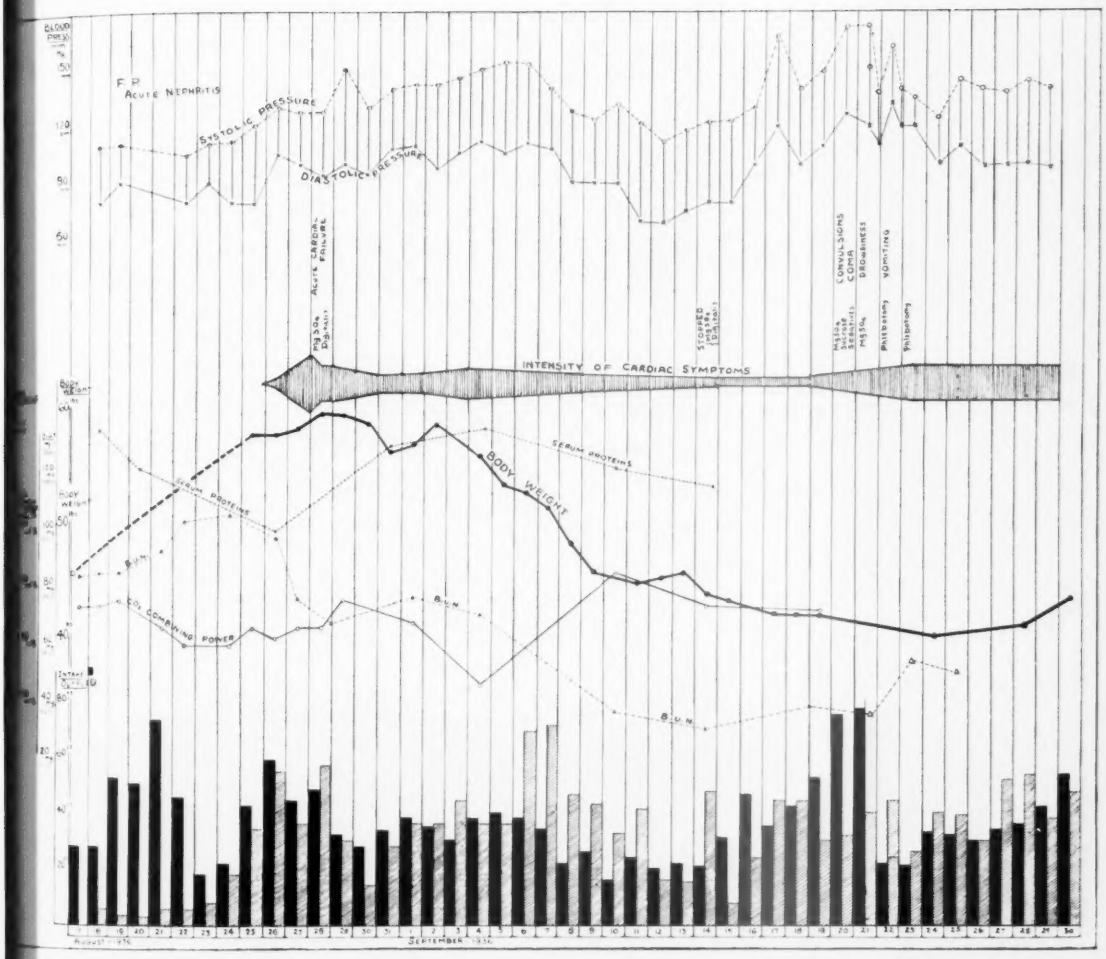

Fig. 12 (case 10).—Chart of a case of acute nephritis with renal failure, cardiac failure, hypertension and encephalopathy, showing severity of symptoms after increase of fluid intake and omission of magnesium sulfate and digitalis.

patients, twelve of whom had signs of frank cardiac decompensation; hypertensive encephalopathy was encountered in five, and uremia in but two. The only two deaths in this entire group were due to acute cardiac failure.

The clinical signs and symptoms of cardiac involvement as they occurred in these cases are described.

A discussion of the factors producing cardiac damage and decompensation is presented. The importance of hypertension as a cause of cardiac decompensation in the patient with acute nephritis is emphasized. Hypertension was observed in all cases in which there was cardiac involvement.

The mode of action of magnesium sulfate and its prophylactic and therapeutic use for the control of the hypertension (vasospasm) in children with myocardial damage are commented on.

A rationale for the limitation of fluids in cases of nephritis with hypertension and cardiac damage has been presented.

Cardiac damage is an immediate danger to life during the acute phase of hemorrhagic nephritis. However, the ultimate prognosis, as regards the heart itself, is good, as only one of twelve surviving patients who had cardiac involvement shows residual cardiac damage.

1740 Bainbridge Street.

DISCUSSION

DR. KENNETH D. BLACKFAN, Boston: Dr. Rubin has pointed out a complication that occurs in acute glomerular nephritis. In about 150 cases in the last ten years my colleagues and I have noted 5 deaths. Two occurred in patients without evidence of cardiac involvement shortly after their admission to the hospital. Three occurred in patients with evidence of renal damage, hypertension and acute congestive heart failure.

For a number of years we have observed that in patients who have acute glomerular nephritis and what we term cerebral manifestations a satisfactory procedure is to keep the hypertension reduced by intramuscular injections of magnesium sulfate, at the same time controlling this temporary effect by administering large amounts of magnesium sulfate by mouth.

The mechanism by which cardiac damage is brought about in acute glomerular nephritis, we have some reason to feel, is based on the toxic effect of the hemolytic streptococcus, particularly as within the past year or so we have observed 5 patients infected with hemolytic streptococci who have exhibited evidence of cardiac damage without renal damage.

It has been quite interesting from our point of view that the patients with acute hemolytic streptococcic infection without renal damage show the clinical manifestations of myocarditis, i. e., dyspnea, gallop rhythm, enlargement of the heart and edema, but histologically we have been unable to discover evidences of the type of myocarditis for which the pathologist usually seeks in the toxic myocarditis caused by the diphtheria bacillus. In these cases we have evidence obtained by electrocardiographic study before, and in several instances after, the damage has subsided.

The point, therefore, is that in streptococcic infections with or without renal damage we do come across evidences of acute congestive heart failure—unrecognizable by the characteristic changes of myocarditis. This raises a question as to the nature of the cardiac changes brought about in acute streptococcic infections.

DR. JOHN D. LYTTLE, New York: Our experience at the Babies Hospital is similar to that of Dr. Rubin and Dr. Rapoport in Philadelphia except that a much larger number of children with acute nephritis show clinical and laboratory evidence of cardiac involvement. I should say that over half of our children who have nephritis show clinical roentgenographic or electrocardiographic evidence of cardiac involvement. The number depends entirely on the eagerness with which one looks for signs.

I believe also that in the majority of these children the damage is slight and will disappear during the period of observation. But we have had 6 patients die for whom cardiac failure was the important cause of death—that is, in approximately 150 cases since 1929. There were 3 autopsies. One patient had pathologic evidence in the heart accounting for the cardiac failure. Two showed no evidence as to what had gone on in the heart to cause failure, nor was there any evidence of vascular damage in other parts of the body.

In the patient who had anatomic changes in the heart the slides presented show, in addition to glomerulonephritis, extensive necrotizing arteritis in the kidney and rheumatic endocarditis and myocarditis. I think this case is unusual and do not believe these changes are commonly found in acute glomerulonephritis. Dr. Lawrence Smith found anatomic changes in the heart in 90 per cent of 59 cases of scarlet fever. He saw these sections and thought the changes were characteristic, but of an extreme degree as compared with what he was accustomed to see in scarlet fever.

As Dr. Blackfan pointed out, I think one has to realize when treating acute nephritis in children that vascular damage can occur in other important viscera, and I think this point deserves more consideration than it generally receives. For instance, Christian recently made the statement that in acute nephritis the circulation is not disturbed sufficiently to warrant any therapeutic measures. I think that is not a correct statement. Basch allows children who have acute nephritis in an early stage to be up and around and to exercise. He has said that this makes the hematuria and albuminuria clear up more quickly. The fact that the majority of children with mild acute nephritis get well promptly and that severe cardiac damage develops only rarely should not allow one to ignore this threat to life.

DR. CHARLES HENDEE SMITH, New York: I should like to bring up one point, not in criticism of the paper but in criticism of a term which is used by both the speaker and by Dr. Blackfan, one which is more or less crystallized in cardiology, but not correct. I refer to "gallop rhythm," a term applied to the triple sound heard at the apex, without any change in rhythm. It should be called "gallop sound" or simply "gallop." To add the word "rhythm" suggests that one is referring to a form of irregularity of the heart beat.

DR. HUGH MCCULLOCH, St. Louis: Dr. Rubin has presented a rather important group of cases in the border zone between cardiac disease and nephritic disease. This group includes conditions varying all the way from malignant hypertension through cardiac disease in the child who has renal injury and nephritis in the child with cardiac injury, to scarlet fever with toxic effect throughout the body. He has emphasized two important manifestations, namely, heart failure and hypertension or at least some change in the blood pressure relationships.

These two conditions, it seems to me, can be adequately correlated if one thinks of the fundamental nature of rheumatic fever and probably of acute hemorrhagic nephritis. That is, the injury is borne by the arteriolar structures in the vessels near the capillary bed of the peripheral circulation; so, if there are injuries in the glomeruli and other small vessels of the kidney and throughout the body, there will be similar injury in corresponding zones of circulation in the cardiac muscle, and in that way one will find signs of myocarditis and probably hypertension in the same patient.

My associates and I have observed this manifestation in our group of cases. The circulatory failure in the nephritic group is somewhat different from the cardiac failure seen in advanced vascular disease or old valvulitis. It is somewhat

similar to the congestive failure in the group with acute progressive rheumatic disease

Dr. Lyttle referred to an interesting thing, which might be emphasized: the rheumatic lesion in the heart muscle known as the Aschoff body or rheumatic nodule, is quite similar to the glomerular lesion of nephritis and includes both crescent formation and other structural injuries in the kidney. In scarlet fever with acute hemorrhagic nephritis plus cardiac injury the nature of the lesion seems to be more than that of toxemia, somewhat like that seen in diphtheria with circulatory collapse rather than congestive failure. Patients who die in the acute stages of scarlet fever are not exactly like the group that Dr. Rubin described.

Dr. Harold L. Higgins, Boston: I should like to ask Dr. Rubin if he does not think the cardiac damage is due to localized edema of the cardiac muscle, a condition analogous to the localized edema one may see in the brain, kidney or skin in acute hemorrhagic nephritis.

Dr. Mitchell I. Rubin, Philadelphia: I should like to thank the various discussers for their interesting comments on this presentation. In answer to Dr. Higgins' question regarding the possibility that the heart failure is due to edema of the heart muscle I should like to state that we have no evidence for this—certainly some of the patients with cardiac damage have no evidence of general edema, and many patients with generalized edema have no manifestations of cardiac damage. Whether or not cardiac failure occurs in the patient with acute hemorrhagic nephritis seems to be more intimately correlated with the presence or absence of vascular spasm (hypertension) than with any other factor.

CRYPTORCHIDISM TREATED WITH GONADOTROPIC PRINCIPLE

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Within the past few years numerous investigators have reported on the treatment of cryptorchidism with the anterior pituitary-like gonadotropic principle of the urine of pregnant women. The number of cases reported by any one observer has in each instance been small. Although the reports as a whole have been extremely favorable, there has arisen justifiable skepticism as regards this form of treatment in a large number of unselected cases. We have been able to treat and study ninety-six unselected patients with cryptorchidism, a series large enough to eliminate any of the chance results of a smaller series. Besides, we have observed and treated several patients with hypoplasia of the genitalia but without cryptorchidism and several with postoperative atrophy of the testicle.

We were able to compare the effects on cryptorchidism and the genitalia of the gonadotropic principle obtained from the anterior lobe of the pituitary gland with those of the gonadotropic principle obtained from the urine of pregnant women in a large series of cases.

GONADOTROPIC PRINCIPLES USED IN THIS STUDY

Of the two gonadotropic principles used in this study, one was obtained from the urine of pregnant women and the other was an extract from the anterior lobe of the pituitary gland. The anterior pituitary-like gonadotropic principle of the urine of pregnant women (antuitrin-S) had a potency of 100 rat units per cubic centi-

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From the Children's Memorial Hospital.

Some patients included in this series were also observed in the clinic of the Northwestern University Medical School.

Presented before the Chicago Pediatric Society, April 20, 1937, and before the American Pediatric Society, April 29, 1937.

The antuitrin-S and the gonadotropic extract of the anterior lobe of the pituitary gland used in this study were furnished by Parke, Davis & Co.

meter. The gonadotropic principle of the anterior lobe of the pituitary gland which we first received had a potency of 10 rat units per cubic centimeter, while that received later assayed from 15 to 18 rat units per cubic centimeter. It also contained from 1 to 3 guinea-pig units per cubic centimeter of thyrotropic principle, which the manufacturers informed us was negligible clinically, as the initial therapeutic dose is in the neighborhood of 50 guinea-pig units.

Parke, Davis & Co. sent us the following information on the two principles employed:

"A direct comparison of the units of Antuitrin-S and the gonadotropic hormone of the anterior pituitary gland cannot be made since the bioassays are based upon somewhat different procedures. Both products are assayed on immature female rats of the same specification—that is to say, 26 to 28 day-old rats are injected twice daily for three days. Ninety-six to 100 hours after starting injections the animals are sacrificed and the ovaries examined for certain changes. In the case of the anterior pituitary gland extract the amount of hormone that will cause an increase in ovarian weight of 100 per cent is designated as one rat unit. This weight increase is due primarily to follicle formation and luteinization. Antuitrin-S causes some increase in gonadal weight but the end point of the assay is not based upon weight increase but rather on the formation of corpora lutea. One rat unit of Antuitrin-S is defined as the minimal quantity of hormone which will cause the formation of corpora lutea in 60 per cent of the test animals at the end of 96 to 100 hours when injected in six doses twice daily for three days. This potency statement can be adapted to the gonadotropic principle of the anterior pituitary by stating that one rat unit is the minimal quantity of hormone which will cause an increase of 100 per cent in the weight of the ovaries of the test animals at the end of 96 to 100 hours when injected in six doses twice daily for three days. Since the biological effect of the gland extract is somewhat different from that obtained following the use of Antuitrin-S there is no rational manner by which the units can be compared.

"On the basis of laboratory assays some workers have claimed that the pregnancy urine extract and the gland extract each contain both the follicle-stimulating and the follicle-luteinizing or gonad-maturing principles, the Antuitrin-S having a preponderance of the luteinizing principle and the gland extract a preponderance of the follicle-stimulating principle. However, this differentiation is not so clear as might be thought on the basis of some of the statements that have been made. Antuitrin-S in large doses will in assay animals induce weight changes in the ovary that can hardly be differentiated from the effect of the anterior pituitary gland fraction. On the other hand, the latter substance will definitely produce more follicular development than the former.

"The anterior pituitary gonadotropic gland extract is obtained from either hog or sheep glands. Antuitrin-S is extracted from human pregnancy urine. From a chemical standpoint not much can be said of either hormone. A solution of gonadotropic principle of the anterior pituitary contains 1 to 2 per cent total solids of which the majority is protein material. In the case of Antuitrin-S the total solid or protein content will average about 0.2 per cent. It is to be expected, therefore, that the latter will be more readily tolerated when given hypodermically."

For purposes of abbreviation the term antuitrin-S will be used to designate the gonadotropic principle of the urine of pregnant women and anterior pituitary extract will be used for the preparation of the gonadotropic principle of the anterior lobe of the pituitary gland employed.

SELECTION OF PATIENTS

All our patients were charity patients attending the outpatient department of the Children's Memorial Hospital. Every boy for whom diagnosis of undescended testicle was made was referred to a special clinic, where he was studied by us. A complete history was taken, and a physical examination was made with emphasis on the location, size and motility of the testicles. For each child a complete blood count was made, and the urine was examined weekly. Photographs were taken, as well as roentgenograms of the wrists. The height and weight were recorded every week. Many of these patients had been under observation for years; so we had notes on the genitalia during that period as well as during treatment and after treatment was discontinued. In none of the children accepted for treatment had there been any progress in the descent of the testicles during the pretreatment period. Progress notes were made weekly.

It was found that care had to be taken in the selection of patients because of the strong cremasteric reflex present at times. Often the testicles were not found in the scrotum when the patient was first undressed, when he was cold or when the scrotum or thigh was touched. At times even at the mere approach of the examiner the testicles would be pulled into the inguinal canal. Often several examinations were made by several attending physicians before a final diagnosis was given. The history was always carefully checked to determine whether the testicles had ever been observed in the scrotum.

Only those patients were selected for treatment of cryptorchidism in whom the testicle could not be palpated or pushed out of the canal or was always found in the inguinal canal but with force could be pushed just through the external ring, with the cord stretched and under tension, so that when the testicle was released it would immediately snap back into the upper portion of the canal. Patients were selected regardless of age. Several obese boys with feminine body build and hypoplasia of the genitalia but without cryptorchidism were also treated.

Of the eighty-nine patients selected for study, sixty-five had unilateral and twenty-four bilateral cryptorchidism, making a total of one hundred and thirteen undescended testicles. Five additional patients had postoperative atrophy of one testicle, and two patients had hypoplasia of the genitalia without cryptorchidism. We found it easier in our recording to consider the number of undescended testicles rather than the number of patients, because in cases of bilateral cryptorchidism the two testicles often did not respond alike.

The patients with cryptorchidism were divided into two main groups, one group of eighteen patients with twenty-two undescended testicles with inadequate treatment or without treatment to serve as controls and the other made up of seventy-one patients with ninety-one undescended testicles whom we feel received sufficient hormone therapy.

OTHER ANOMALIES ACCOMPANYING CRYPTORCHIDISM

Hypospadias was present in five boys, ventral hernia in two and cleft palate, cretinism and arthrogryposis multiplex congenita in one each. Hydrocele was present on the right in four boys. In only one boy was the hydrocele on the same side as the cryptorchidism, and in this case the testicle descended into the upper portion of the scrotum, and the hydrocele disappeared.

METHOD OF TREATMENT

Patients were selected for treatment with antuitrin-S or anterior pituitary extract alternately or in groups. In a few cases alternate doses of antuitrin-S and anterior pituitary extract were used. In some cases, if after an extended course of treatment with one extract no results were observed, the other extract was tried.

As the rat unit content per cubic centimeter of antuitrin-S was 100 while that of the anterior pituitary extract was only 10 or 15, it was impossible to give the latter in as large doses as the former. The manufacturers suggested that we try to use the two extracts cubic centimeter for cubic centimeter rather than on the basis of rat units. The size of the individual doses varied for different patients without relation to age. We usually started with 0.5 cc. of the extract two or three times a week, increasing the dose by 0.5 cc. at succeeding injections until the desired amount had been given or until an unfavorable reaction had occurred. The largest individual dose was 6 or 7 cc. three times a week, given to a 13 year old patient. There was maintained a dose of from 1 to 3 cc. for forty-two patients, from 3 to 4 cc. for 19, from 4 to 5 cc. for five and from 5 to 7 cc. for five. The injections were given two or three times a week for varying lengths of time up to several months.

Rest periods during the course of treatment were tried in some cases. Thirty-one boys had one or more rest periods, and thirty-nine had no rest periods. For six boys the rest period lasted one month or less; for sixteen, from one to four months; for six, from four to six months, and for four, for over six months.

Both the subcutaneous and the intramuscular route of injection were used—the former in the deltoid region and the latter deep in the buttocks.

Thyroid Medication: Thyroid in doses of 1 to 2 grains (0.06 to 0.12 Gm.) daily was given in conjunction with the gonadotropic principle to ten patients with cryptorchidism. Five of these patients were obese, with small genitalia as well as cryptorchidism. A feminine type of body build accompanied the obesity in two cases. For these five patients, there was complete descent of the testicles in three, partial descent in one and no change in one. Increase in the size of the testicles occurred in three patients. No change in body build was noted.

Four of the ten patients had a normal body build. In none of these did descent of the testicles occur. One child was a cretin; and although the hypothyroidism was benefited, no change was noted in the size or location of the testicles.

The thyroid administered may have enhanced the effect of the gonadotropic principle for the obese patients, but it seemed of no value to patients with a normal build or to those with a feminine build.

EFFECT OF THE GONADOTROPIC PRINCIPLE ON THE SIZE OF THE TESTICLE

Measurements of the testicles, estimated as accurately as possible, were recorded at the time of each examination in order to ascertain what effect treatment had on size and firmness. As a general rule most of the testicles that showed some descent during treatment also became somewhat larger and firmer. They returned to their former condition during rest periods and after treatment was discontinued. In no case did atrophy of a testicle occur as a result of treatment, nor did enlargement above normal ever last.

1. *Normal Testicles.*—In seventeen patients with cryptorchidism there was an increase in the size of what we considered normal-sized testicles, as illustrated in the following two cases. The testicles of an 11 year old boy measured 3 by 2 cm. before treatment, but during treatment they increased to 4 by 3 cm. In a 3 year old boy there was an increase from 1.5 by 1 cm. to 3 by 2.5 cm. In some of the other children the increase in size was not so marked. The increase in size occurred equally in the two testicles in all but three patients. In these it was more pronounced on the side where the testicle was undescended and was accompanied with descent. In seven patients there was complete descent of the testicles; in five, partial descent, and in five, no change. In only two of these seventeen patients did enlargement of the penis also occur. After treatment was discontinued the testicles returned to normal size, and atrophy never followed.

Nine of these patients received antuitrin-S; three, anterior pituitary extract, and five, both extracts.

2. *Small Testicles.*—Seven patients with cryptorchidism had testicles that we considered smaller than normal. In three of these children the penis was small, and there was obesity, with a feminine type of body build. In two of these three boys the testicles increased to normal size, with slight enlargement of the penis, while in the third there was no change. There was no change in body build. Of five undescended testicles, one completely descended, three partially descended and one showed no change.

The other four patients had a normal body build, with a small penis in two and a normal-sized penis in two. In only one of these four did the testicles increase to normal size, while in the others there was no change. There was no change in the size of the other parts of the external genitalia. Of four undescended testicles, three descended and one remained unchanged.

Two more patients with marked hypoplasia of the external genitalia were treated with the gonadotropic principle but are not included here because they did not have cryptorchidism. One was obese, with a feminine type of body build, while the other had a normal body build. The only change after extensive treatment was a slight increase in the size of the testicles of the obese child.

From the foregoing observations it appears that in boys with hypogonadism the gonadotropic principle has no effect on body build and little effect on descent of the testicles, but it does seem to cause some enlargement of the testicles. In obese boys without a feminine type of body build, enlargement and descent of the testicles are more apt to occur, although obesity is not influenced.

3. *Atrophy of the Testicles.*—We had the opportunity to study the effect of treatment on six testicles that showed postoperative atrophy. Three patients had had bilateral cryptorchidism, with operation on one side previous to the time that we started treatment for the remaining undescended testicle. In each of them the atrophic testicle was small and hard and through the external ring in the upper part of the scrotum. Treatment with the gonadotropic extracts had no effect on the atrophic testicle. In only one patient did the testicle descend, and in none of them did enlargement occur, although only two of them were of normal size.

EFFECT ON THE SIZE OF THE SCROTUM AND PENIS

The scrotum was always much smaller than normal when bilateral cryptorchidism was present. In the patients with unilateral cryptorchidism the scrotum was normal in size or moderately smaller on the affected side. For thirteen of the twenty-four boys in whom the scrotum was definitely smaller than normal before treatment, there was an increase in size during treatment. For these thirteen, there was descent of the testicle in ten, and there was no change in three. Enlargement of a previously normal-sized scrotum occurred in three patients, together with enlargement of the penis. In only ten of the sixteen patients with scrotal enlargement did enlargement of the penis also occur. An increase in the size of the testicles as well as of the scrotum occurred in eight patients.

We thought the penis was definitely smaller than normal in fifteen boys. In five of these (two obese and three otherwise normal boys), all under 6 years of age, an increase in the size of the penis occurred during treatment. Although the increase was beyond normal in two boys, the penis of each of them had returned to normal size or had remained normal in size when observed several months after treatment. Descent of the testicles occurred in three of the five boys with enlargement of the penis and in only three of those with a small penis.

In eight boys, 6 years of age or less, there was a definite increase in the size of a previously normal-sized penis. This was accompanied with descent of the testicles in five. In two boys the penis has returned to normal size, in two it is only slightly larger than before treatment while in four there is still considerable enlargement. For example, in one 3 year old boy the penis became about the size of that of an 8 year old boy. Six months after treatment was discontinued it has regressed in size to about that of a 6 year old boy.

About an equal number of these boys received antuitrin-S and anterior pituitary extract. When enlargement of the penis takes place there is always flushing of the genitalia. It appears that a boy 6 years of age or less with an apparently normal-sized penis is more apt to show enlargement of the penis than is an older boy.

EFFECT ON DESCENT OF THE TESTICLE

It is somewhat difficult to estimate accurately the final results of treatment because of the numerous factors which must be taken into consideration. It must be considered whether or not the testicle could be reduced through the external ring previous to treatment, whether the testicle descended into the scrotum to remain only part of the time or throughout the period of treatment or whether the descended testicle continued in the scrotal position after treatment was discontinued. In recording our observations we classified our results as follows: no change, when the testicle remained in its former location; partial descent, when it descended into the middle or lower portion of the scrotum to remain part of the time or when it descended from a nonpalpable abdominal position to a palpable position in the canal, and complete descent, when the scrotal position was maintained. We found that a period of observation after treatment had been discontinued was necessary. A testicle that remains in the scrotum at the end of treatment may ascend into the canal again later, but in our experience descent never occurred spontaneously after treatment had been discontinued.

The patients were divided into groups according to the form of gonadotropic extract administered.

Treatment with Anterior Pituitary Extract (table 1).—There were thirty-two patients, with forty undescended testicles, in the group treated with the gonadotropic principle derived from the anterior lobe of the pituitary gland. When treatment was discontinued, twenty-six testicles were apparently unchanged in location, four were partially descended and ten were completely descended. On further observation for varying lengths of time after treatment had been discontinued, the same twenty-six again showed no change, but only seven were completely descended and seven were classified as partially descended. If all the observations had been made the same length of time after treatment had been stopped, it is possible that more than three of the completely descended testicles would have shown some retraction back into the inguinal canal.

None of the five nonpalpable testicles became palpable. Nineteen testicles were reducible just through the external ring (not remaining in the scrotum) before treatment. During treatment eight of these completely descended, but on further observation only five remained completely descended. Only one of the nonreducible testicles descended completely.

Bilateral cryptorchidism was present in eight patients. In six of these the effect on the two testicles was the same, while in each of two patients only one testicle descended partially.

TABLE 1.—*Patients Treated with the Gonadotropic Extract of the Anterior Lobe of the Pituitary Gland* *

Case Number	Age of Patient, Years	General Body Build	Location of Testicles Before Treatment			Reducible Before Treatment		Total Amount of Extract, Cc.	Total Rat Units	Total Number of Injections	Total Time of Treatment and Rest Periods, Months	Rat Units Given Before Change Was Noted	Location of Testicles After Treatment			Time of Observation, Months		Final Results		
			Unilateral Cryptorchidism	Bilateral Cryptorchidism		Right Side	Left Side						Unilateral Cryptorchidism	Bilateral Cryptorchidism		Before Treatment	After Treatment	Unilateral Cryptorchidism	Bilateral Cryptorchidism	
				Right	Left									Right	Left				Right	Left
1	11	Normal	.....	IC	IC	No	Yes	19.5	295.5	10	2.00	.....	...	IS	IS	0.50	3	...	IS	IS
2	10	Normal	L,IC	...	...	....	No	132.0	1,320.0	53	5.00	710.0	IC	...	...	48.00	8	MC	...	...
3	11	Normal	L,NP	...	...	....	No	48.0	720.0	18	3.00	.....	NP	...	...	0.75	1	NP	...	...
4	2	Normal	R,NP	...	...	No	....	25.0	375.0	13	1.00	.....	NP	...	...	1.00	1	NP	...	...
5	9	Normal	R,UC	...	...	No	....	60.0	795.0	30	4.00	.....	NP	...	...	0.25	1	NP	...	...
6	10	Normal	.....	IC	IC	Yes	Yes	40.0	700.0	19	1.75	.....	...	IC	IC	0	1	...	IC	IC
7	8	Normal	L,UC	...	...	....	No	66.0	990.0	23	2.00	810.0	IC	...	...	0	1	MC	...	...
8	8	Normal	L,UC	...	...	....	No	61.0	916.0	22	7.00	.....	UC	...	...	0	1	UC	...	...
9	5	Normal	L,UC	...	...	....	Yes	96.5	965.0	40	4.00	200.0	IS	...	...	5.50	5	IS	...	...
10	6	Normal	.....	LC	LC	Yes	Yes	82.0	820.0	44	2.50	520.0	...	IS	IS	35.00	9	...	IS	IS
11	12	Normal	R,MC	...	...	No	....	44.0	735.0	18	6.00	.....	LC	...	...	0	1	LC	...	...
12	1	AMC	.....	NP	MC	No	No	67.2	672.5	33	2.75	.....	...	NP	MC	4.00	1	...	NP	MC
13	10	Normal	L,IC	...	...	....	Yes	30.0	445.0	13	8.00	.....	IC	...	...	0	3	LC	...	...
14	9	Normal	.....	IC	IC	No	Yes	145.0	1,450.0	64	2.25	600.0	...	LC	IS	6.00	6	...	MC	MC
15	6	Normal	L,IC	...	...	No	....	82.0	1,230.0	28	9.00	52.0	LC	...	...	0.25	1	LC	...	...
16	2	Normal	L,NP	...	...	....	No	81.0	1,215.0	30	6.00	.....	NP	...	...	0.25	1	NP	...	...
17	1	Cretin	R,NP	...	...	No	....	70.5	1,057.5	32	5.50	.....	NP	...	...	17.50	1	NP	...	...
18	3	Normal	R,LC	...	...	Yes	....	95.0	1,470.0	43	2.00	.....	LC	...	...	38.00	1	LC	...	...
19	4	Normal	R,UC	...	...	No	....	30.5	305.0	17	8.50	.....	UC	...	...	0	10	UC	...	...
20	5	Normal	R,LC	...	...	No	....	100.5	1,005.0	47	4.00	22.5	LC	...	...	33.00	1	LC	...	...
21	3	Obese	.....	UC	UC	No	Yes	115.0	1,725.0	42	2.00	.....	...	UC	MC	39.00	1	...	UC	LC
22	9	Obese	L,IC	...	...	....	No	26.0	260.0	16	2.50	.....	LC	...	...	0	1	IC	...	...
23	6	Obese	R,LC	...	...	Yes	....	41.0	410.0	25	11.00	.....	IS	...	...	11.00	10	IS	...	...
24	6	Thin	R,IC	...	...	Yes	....	62.0	635.0	34	11.00	.....	IS	...	...	65.00	2	IS	...	...
25	8	Normal	.....	IC	IC	Yes	No	53.0	530.0	20	3.50	.....	...	IS	IC	0	3	...	OP	OP
26	7	Normal	.....	IC	IC	Yes	Yes	147.0	1,595.0	55	6.00	.....	...	IC	IC	9.00	1	...	OP	OP
27	10	Normal	R,IC	...	...	No	....	104.0	1,560.0	35	3.00	.....	IC	...	...	89.00	2	OP	...	...
28	11	Normal	L,IC	...	...	....	Yes	156.0	1,610.0	66	7.00	.....	LC	...	...	60.00	1	OP	...	...
29	10	Obese	L,MC	...	...	....	No	126.0	1,890.0	43	3.50	120.0	LC	...	...	30.00	1	LC	...	...
30	7	Stocky	R,IC	...	...	Yes	....	74.0	740.0	35	5.50	.....	LC	...	...	3.00	9	LC	...	...
31	10	Normal	L,IC	...	...	....	Yes	116.0	1,160.0	27	3.50	.....	LC	...	...	16.00	1	IC	...	...
32	10	Normal	R,IC	...	...	Yes	....	55.5	555.0	30	3.50	25.0	IS	...	...	0	9	IC	...	...

* In tables 1 to 3 and 6 NP indicates nonpalpable; IC, inguinal canal; UC, upper portion of the canal; MC, midportion of the canal; LC, lower portion of the canal; OP, operated on; IS, in scrotum; R, right; L, left; AMC, arthrogryposis multiplex congenita.

Antuitrin-S Treatment (table 2).—The gonadotropic principle of the urine of pregnant women was used in the treatment of twenty-three boys with thirty-one undescended testicles. At the end of the treatment twelve testicles were not changed in location, four were partially descended and fifteen were completely descended. On further observation for varying lengths of time after treatment had been discontinued, the same twelve were unchanged, only fourteen were completely descended and five were classified as partially descended.

Three of seven nonpalpable testicles became palpable in the canal. Before treatment six testicles were reducible just through the external ring (not remaining in the scrotum). Five of these descended completely, but on later observation only four remained completely descended. The remaining ten completely descended testicles had not been reducible.

Bilateral cryptorchidism was present in eight patients. In three of these the two testicles reacted similarly, while in five there was complete descent on one side and no change on the other.

When descent of the testicle did occur, it began after the patient had received from 1,000 to 8,000 rat units; two thirds of the patients showed improvement after receiving 4,000 rat units.

Treatment with Both Anterior Pituitary Extract and Antuitrin-S (table 3).—Both gonadotropic extracts were used in the treatment of sixteen boys with twenty undescended testicles. Some of these boys received alternating doses of the two extracts, while the others were first given one extract, and after a period of treatment without apparent results the other extract was used. At the end of the treatment ten testicles remained unchanged, eight had completely descended and two had partially descended. Further observation after discontinuance of treatment showed that nine remained unchanged, five were completely descended and six were partially descended. Three of six nonpalpable testicles became palpable and partially descended. One of the two testicles that were reducible before treatment descended completely.

RESULTS ACCORDING TO RAT UNITS RECEIVED

In table 4 the testicles of the patients who received adequate treatment have been divided according to the total number of rat units received. They have been further grouped according to whether antuitrin-S or anterior pituitary extract was administered.

Antuitrin-S was used in the treatment of thirty-one undescended testicles. At the conclusion of treatment fifteen (48 per cent) were in the scrotum, but on further observation some time later only fourteen (45 per cent) remained descended. If the testicles that were partially descended are included, the number benefited would be nineteen (61 per cent).

TABLE 2.—*Patients Treated with Gonadotropic Extract of Urine of Pregnant Women (Antuitrin-S)*

Case Number	Age of Patient, Years	General Body Build	Location of Testicles Before Treatment			Reducible Before Treatment		Total Amount of Antuitrin-S, Cc.	Total Rat Units	Total Number of Injections	Total Time of Treatment and Rest Periods, Months	Rat Units Given Before Change Was Noted	Location of Testicles After Treatment			Time of Observation, Months		Final Results		
			Unilateral Cryptorchidism	Bilateral Cryptorchidism		Right Side	Left Side						Unilateral Cryptorchidism	Bilateral Cryptorchidism		Before Treatment	After Treatment	Unilateral Cryptorchidism	Bilateral Cryptorchidism	
				Right	Left									Right	Left				Right	Left
33	2	Normal	.....	LC	UC	Yes	No	105.0	10,500	50	9.50	4,200	...	IS	UC	0.25	6	...	IS	UC
34	9	Normal	.....	LC	LC	No	No	32.5	3,250	23	6.00	1,300	...	IS	IS	0	6	...	IS	IS
35	10	Short	R,IC	...	...	Yes	....	19.0	1,900	14	5.00	1,100	IS	...	...	0	1	IS	...	...
36	10	Normal	L,NP	...	...	....	No	68.5	6,850	29	4.50	2,800	MC	...	...	0	11	UC	...	...
37	11	Normal	L,NP	...	...	....	No	125.0	12,500	62	5.50	.....	IS	...	...	0	8	IS	...	...
38	7	Normal	R,IC	...	...	Yes	....	73.0	7,300	40	8.00	0	IC	...	...	0	3	IC	...	...
39	12	Obese	R,UC	...	...	No	....	26.5	26,500	18	2.00	1,450	IS	...	...	1.00	11	IS	...	...
40	9	Normal	R,MC	...	...	No	....	65.0	6,700	23	3.50	6,500	IS	...	...	1.00	5	IS	...	...
41	4	Short	L,NP	...	...	....	No	28.5	2,850	17	2.00	0	NP	...	...	0	12	NP	...	...
42	4	Normal	R,LC	...	...	Yes	....	22.0	2,200	14	3.50	2,200	IS	...	...	0	11	LC	...	...
43	8	Normal	.....	UC	LC	No	Yes	135.0	13,500	74	22.00	3,900	...	LC	IS	0	1	...	LC	IS
44	6	Normal	R,IC	...	...	No	....	66.5	6,650	30	12.00	4,450	LC	...	...	19.00	1	LC	...	...
45	12	Normal	R,LC	...	...	No	....	90.0	9,000	55	5.25	2,400	IS	...	...	0	1	IS	...	...
46	6	Normal	.....	IC	IC	No	No	111.0	11,100	43	8.75	.....	...	IS	LC	0	1	...	IS	MC
47	9	Normal	R,LC	...	...	No	....	19.5	1,950	13	18.00	900	IS	...	...	0	16	IS	...	...
48	2	Stocky	R,LC	...	...	No	....	43.0	4,300	29	3.00	1,250	IS	...	...	13.00	7	IS	...	...
49	13	Normal	L,LC	...	...	....	No	37.0	3,700	19	5.00	0	IC	...	...	0	1	OP	...	...
50	4	Normal	.....	LC	MC	Yes	No	106.0	10,600	46	5.50	8,250	...	IS	IC	1.00	4	...	IS	OP
51	6	Thin	L,NP	...	...	....	No	116.0	11,600	48	5.00	0	NP	...	...	36.00	2	OP	...	...
52	11	Normal	L,NP	...	...	....	No	124.5	12,450	53	7.00	.....	UC	...	...	30.00	1	OP	...	...
53	12	Normal	.....	NP	IC	No	No	118.0	11,800	57	6.00	.....	...	NP	LC	0	6	...	OP	OP
54	12	Normal	.....	MC	NP	No	No	202.5	20,250	68	13.00	7,150	...	MC	NP	0	6	...	UC	OP
55	4	Normal	.....	NP	LC	No	No	88.0	8,800	54	9.00	.....	...	LC	IS	24.00	1	...	OP	IS

TABLE 3.—*Patients Treated with Both Gonadotropic Extracts*

Case Number	Age of Patient, Years	General Body Build	Location of Testicles Before Treatment			Reducible Before Treatment		Total Amount of Extract, Cc.	Total Rat Units of Anterior Pituitary Extract	Total Rat Units of Antuitrin-S	Total Number of Injections	Total Time of Treatment and Rest Periods, Months	Location of Testicles After Treatment			Time of Observation, Months		Final Results		
			Unilateral Cryptorchidism	Bilateral Cryptorchidism		Right Side	Left Side						Unilateral Cryptorchidism	Bilateral Cryptorchidism		Before Treatment	After Treatment	Unilateral Cryptorchidism	Bilateral Cryptorchidism	
				Right	Left									Right	Left				Right	Left
56	4	Stocky	.....	IC	UC	No	No	58.0	420.00	1,600	39	9.00	...	IS	IS	52.00	1	...	IS	IS
57	10	Normal	L,UC	...	...	....	No	213.0	1,100.00	10,300	86	10.00	IS	...	...	0.25	3	IS	...	...
58	10	Obese	.....	NP	NP	No	No	196.5	1,380.00	7,450	122	20.00	...	IS	IS	0.25	1	...	LC	LC
59	4	Stocky	R,MC	...	...	No	....	31.0	270.00	400	18	3.00	LC	...	...	0.25	6	UC	...	...
60	10	Obese	.....	UC	UC	No	No	177.0	1,760.00	2,300	53	13.50	...	IS	MC	61.00	1	...	IC	MC
61	11	Normal	R,MC	...	...	No	....	136.7	867.75	5,000	57	7.00	MC	...	...	0	1	MC	...	...
62	13	Normal	R,LC	...	...	Yes	....	52.5	395.00	1,300	17	5.75	IC	...	...	10.00	3	IS	...	...
63	9	Normal	L,LC	...	...	....	No	131.0	1,210.00	1,000	55	5.00	LC	...	...	0	3	OP	...	...
64	7	Normal	R,LC	...	...	No	....	195.0	815.00	9,550	94	10.00	NP	...	...	0	1	OP	...	...
65	9	Normal	R,LC	...	...	No	....	158.0	1,035.00	7,000	76	14.00	LC	...	...	3.00	1	OP	...	...
66	3	Stocky	R,NP	...	...	No	....	141.0	280.00	11,300	82	18.00	IS	...	...	2.00	4	OP	...	...
67	8	Normal	.....	NP	LC	No	Yes	119.0	1,650.00	900	42	3.25	...	NP	LC	34.00	1	...	NP	OP
68	5	Stocky	L,NP	...	...	....	No	155.0	510.00	10,350	78	13.50	NP	...	...	0	2	OP	...	...
69	6	Normal	L,NP	...	...	....	No	186.0	120.00	2,193	84	16.25	NP	...	..	0	1	OP	...	...
70	12	Normal	L,LC	...	...	....	No	107.0	870.00	2,000	34	11.00	IS	...	...	15.00	4	IS	...	...
71	7	Normal	L,MC	...	...	....	No	117.0	1,150.00	2,300	47	10.75	MC	...	...	27.00	1	MC	...	...

Of forty undescended testicles of the patients who received anterior pituitary extract ten (25 per cent) completely descended during treatment, but only seven (18 per cent) remained descended after further observation. By including the partially descended testicles the number benefited would be fourteen (35 per cent).

Both antuitrin-S and anterior pituitary extract were used in the treatment of twenty undescended testicles. Eight of these (40 per cent) were descended at the conclusion of treatment, but further observation some time later showed that only five (25 per cent) had remained descended. Eleven (55 per cent) were benefited, if the partially descended testicles are included.

TABLE 4.—*Results of Treatment According to Rat Units Administered*

Extract used.....	Antuitrin-S				Both Extracts				Anterior Pituitary Extract					
Total rat units administered.....	1,000 to 4,000	4,000 to 8,000	8,000 to 13,000	13,000 to 22,000	900 to 3,000	3,000 to 8,000	8,000 to 12,000	12,000 to 25,000	150 to 400	400 to 700	700 to 900	900 to 1,100	1,100 to 1,500	1,500 to 1,900
Number of testicles	10	5	12	4	9	4	5	2	5	8	8	5	7	7
Reducible before treatment.....	3	1	2	1	1	..	..	..	1	5	5	1	3	4
No change.....	4	1	5	2	5	2	1	2	3	4	5	3	5	6
Partial descent.....	..	2	2	..	1	1	..	..	..	..	2	1	..	1
Complete descent by end of treatment.....	6	2	5	2	3	1	4	..	2	4	1	1	2	..
Descended at end of treatment, percentage.....	60	40	41	50	44	25	80	0	40	50	12	20	28	0
Final percentage of descended testicles	50	40	41	50	44	0	20	0	40	25	12	20	14	0
Total percentage benefited.....	60	80	58	50	55	50	80	0	40	50	37	40	28	14

The results obtained with antuitrin-S compare favorably with those obtained with both antuitrin-S and anterior pituitary extract. It will be noted that the patients of both these groups received approximately the same total number of rat units. This was possible because of the comparatively large amounts of antuitrin-S administered to the latter group. Also, from tables 2 and 3 it can be seen that in both groups, if descent was to take place, improvement usually was noted when from 1,000 to 4,000 rat units had been administered. Descent at the end of treatment occurred in 48 per cent of the patients who received antuitrin-S, as compared to 40 per cent of the group receiving both antuitrin-S and anterior pituitary extract, while improvement was noted in 61 and 55 per cent, respectively. This is far superior to the results obtained when only anterior pituitary extract was used, 25 per cent descending during treatment and 35 per cent showing improvement. Our only explanation for this is in the number of rat units administered. The patients who received anterior pituitary extract were under treat-

ment as long and received as many injections and cubic centimeters of extract on the average as those who received antuitrin-S, but the rat unit content of the former was only from 10 to 15 per cubic centimeter, while that of the latter was 100. Consequently, the patients who were given anterior pituitary extract rarely received as many total rat units as those who were given antuitrin-S, because of the large amount of material that would have had to be given to equalize the rat units. That anterior pituitary extract is active and has some effect on the external genitalia seems to be amply demonstrated by the fact that it produced descent of the testicles in some instances and at times caused an increase in the size of the testicles, penis and scrotum. Its value might be enhanced by raising the rat unit content of the gonadotropic principle, if the thyrotropic principle did not prove deleterious with this concentration.

As far as we could observe there was no difference between the subcutaneous and the intramuscular route of administration of either extract. However, the children objected more to the latter type of injection. As to the size of the individual doses, we found that local and general reactions were more likely to occur when large doses, of from 5 to 7 cc., were used. The results of treatment seemed to depend more on the total number of rat units administered than on the size of the individual dose. It seems that administering from 2 to 3 cc. of antuitrin-S two or three times a week is the most advantageous method of treatment. Many of the children were given rest periods during the course of treatment. We could observe no advantages from this; in fact, in some cases there was definite, although temporary, regression of progress during these periods.

There were five obese patients, with eight undescended testicles, in the whole series. Five of these patients were treated with antuitrin-S or with both extracts, and descent occurred in three but was not maintained. Descent did not occur in three patients treated with anterior pituitary extract.

In the cases in which thyroid also was used, this drug did not seem to enhance the gonadotropic principles in producing descent or change in the testicles.

RESULTS ACCORDING TO AGE

In table 5 all the patients with cryptorchidism who received treatment have been divided according to the patients' ages. No separate listing is made for treatment with antuitrin-S or anterior pituitary extract, because in the two groups there was a fairly equal distribution through the various ages. In 36 per cent of twenty-two undescended testicles of the group of boys from 1 to 5 years of age there was com-

plete descent at the conclusion of treatment. On observation some time after treatment 27 per cent had remained descended. For the group of boys from 5 to 9 years old, 34 per cent of the testicles were completely descended at the conclusion of treatment, but only 28 per cent remained descended. Adding the partially descended testicles, the number benefited would be eleven (38 per cent). For the group of boys from 9 to 14 years old the figures were 43, 33 and 58 per cent, respectively. If those treated with antuitrin-S were considered separately, these percentages would all be higher, and the relative relationship between the various age groups would be the same (table 5). Therefore, it seems that treatment at any time after the first year of life may be successful. But when the effect on the penis is considered, it must be remembered

TABLE 5.—*Results of Treatment According to Age of Patient*

Age, years	1	2	3	4	5	6	7	8	9	10	11	12	13	Total
Undescended testicles	3	5	4	10	3	10	6	10	10	13	8	7	2	91
Position before treatment														
Nonpalpable	2	2	1	2	1	2	1	1	..	3	1	2	..	18
In canal	1	3	3	8	2	8	5	9	10	10	7	5	2	73
Testicles reducible	..	1	2	2	1	4	4	3	1	6	2	..	1	27
Complete descent after treatment	..	2	1	4	1	5	1	3	5	4	3	3	2	34
Complete descent after observation period	..	2	..	4	1	4	..	2	4	2	3	3	1	26
Partial descent	..	..	..	3	..	..	..	1	1	3	1	1	..	10
No change	3	3	3	3	2	5	5	6	4	6	3	4	..	47
Descended at end of treatment, percentage	Antuitrin-S..56 Total.....36				Antuitrin-S..43 Total.....34				Antuitrin-S.....47 Total.....43					
Final percentage with complete descent	Antuitrin-S..44 Total.....27				Antuitrin-S..43 Total.....28				Antuitrin-S.....47 Total.....33					

that enlargement of a normal-sized penis is more likely to occur when the boy is 6 years of age or younger. Taking this into consideration, we feel that treatment should not be started until the boy is at least 7 years of age. The size of the individual dose and the total number of rat units administered before descent of the testicle takes place do not seem to bear any relationship to the age of the patient.

CONTROL GROUP OF PATIENTS

A separate group of eighteen patients with twenty-two undescended testicles not included in the series of patients treated was also studied (table 6). This will serve as a control group, because the patients were observed over about the same period as those who received treatment, and they had comparatively the same degree of cryptorchidism. In five instances (four patients) the testicle was in the canal part of the time but could be easily reduced to the lower portion of the scrotum, where it remained for a varying length of time. After the administration of from 150 to 1,250 rat units of antuitrin-S, these five testicles remained

in the scrotum permanently. This demonstrates the good results that can be obtained easily if this type of patient is selected for treatment. Two other children (4 and 9 years of age respectively), each with one reducible testicle similar to those just mentioned, were not given any treatment but were observed over a nine month period. In the younger child there was no change in the position of the testicle, and in the older child the testicle now remains in the scrotum most of the time. Twelve patients, with fifteen undescended testicles, were inadequately treated with GHP, receiving only from 5 to 290 rat units. Treatment was stopped because of lack of cooperation or because of the wishes of the parents. However, these patients returned for examination over about

TABLE 6.—*Control Series of Patients*

Case Number	Age of Patient, Years	General Body Build	Location of Testicles on First Examination		Reducible Before Treatment		Total Rat Units	Total Number of Injections	Total Time of Observation, Months	Location of Testicles After Treatment and Observation Period	
			Right	Left	Right	Left				Right	Left
72	6	Normal	MC	...	No	....	50	5	45.00	MC	...
73	8	Normal	...	LC	....	Yes	300	3	6.00	...	IS
74	11	Obese	LC	LC	Yes	Yes	1,250	8	11.50	IS	IS
75	10	Normal	...	IC	....	Yes	150	2	10.00	...	IS
76	11	Normal	...	LC	....	Yes	750	6	9.00	...	IS
77	1	Normal	...	IC	....	No	20	2	6.00	...	NP
78	9	Normal	IC	...	No	....	80	5	8.00	IC	...
79	9	Normal	IC	...	No	....	290	8	0.25	IC	...
80	6	Normal	IC	IC	Yes	Yes	20	2	10.00	IC	IC
81	3	Normal	...	IC	....	No	135	5	1.00	...	NP
82	5	Normal	IC	IC	Yes	Yes	45	5	43.00	IC	IC
83	7	Normal	IC	...	No	....	35	3	85.00	IC	...
84	7	Normal	IC	...	Yes	....	15	2	1.00	IC	...
85	2	Normal	NP	...	No	...:	65	5	1.00	NP	...
86	5	Normal	...	NP	....	No	5	1	13.00	NP	...
87	8	Normal	IC	IC	Yes	Yes	10	1	14.00	IC	IC
88	4	Normal	IC	...	Yes	....	0	0	9.00	IC	...
89	9	Normal	IC	...	Yes	....	0	0	3.00	IS	...

the same period as those who were adequately treated. In none of them was there any change in the location of the testicle, although in five the testicle could be reduced through the external ring (not remaining in the scrotum) at the beginning of observation. In none was there any change in the size of the penis, scrotum or testicles. Though this control group of patients is small, it emphasizes clearly that the gonadotropic principle produces changes in the genital system leading to descent of the testicle in some patients in whom these changes would not have taken place over the same period.

EFFECT OF TREATMENT ON HERNIA

It was interesting to note the effect the gonadotropic extracts had on inguinal hernia. Inguinal hernia was present in fifteen of the boys at the beginning of treatment and was still present in fourteen at the con-

clusion of treatment. In one boy the hernia decreased in size. Descent of the testicle occurred in five of the boys with hernia. The hernia which disappeared during treatment did not recur during a further period of observation. Descent of the testicle did not take place in this boy. The hernia was on the same side as the cryptorchidism in fourteen instances.

An inguinal hernia became noticeable on the same side as the cryptorchidism in five boys during treatment when no hernia (or history of hernia) had been noticed previously. In three there was descent of the testicle and in two partial descent at the conclusion of treatment.

In one patient inguinal hernia which had been present since early infancy disappeared when the age of 3 years was reached. A truss had been worn. During treatment there was descent of the testicle, with no recurrence of the hernia. Another patient had had a strangulated inguinal hernia during infancy which was reduced without operation. No hernia was noticed at the beginning, during or after treatment with gonadotropic principle. As the testicle failed to descend during treatment, an operation was performed, and a small hernia was observed, with many adhesions to the spermatic cord fixing the testicle in the inguinal canal.

EFFECT OF TREATMENT ON BODY BUILD

Five of the seventy-one treated patients were obese, while the others were either thin or stocky or had a normal body build. Three of the obese patients had a distinctly feminine type of body build. There was also one obese boy without cryptorchidism, who had hypoplasia of the genitalia and a feminine type of body build. He received 5,566 rat units of both gonadotropic extracts over a period of seven and one-half months. The basal metabolic rate of the obese children was as low as minus 21. In none of the treated children was there any change in the type of body build, either during the course of treatment or during the later period of observation.

Many of these children had been in the clinic for many months before treatment, so there was a prolonged period of observation of their height and weight. Although the data have not been completely analyzed, because a longer period of observation is necessary, it is our impression that about the same rate of increase in height and weight was maintained during and after treatment as had been present before. When thyroid was administered and the diet restricted, the weight of the obese patients could be held stationary or could even be decreased. This had no influence on the effect of the gonadotropic extracts on the testicles.

EFFECT ON PUBERTY

It was difficult to estimate what effect treatment had on the development of puberty. One or more of the changes that normally occur during puberty developed in fourteen of the boys. In six of these (five aged 13 years and one aged 12 years) there was a fairly profuse growth of coarse pubic hair, accompanied with changes in the voice but without enlargement of the genitalia; in three there was descent of the testicles. A moderate growth of coarse to fine pubic hair accompanied with enlargement of the penis occurred in four boys (12, 8, 4 and 3 years of age, respectively); in three there was descent of the testicles. The pubic hair disappeared, and the penis returned to normal size in the 3 year old boy after treatment was discontinued, but in the others the changes, though less marked, are still present. In the four remaining patients (11, 11, 8 and 4 years of age, respectively) the only pubertal change was the development of a moderate coarse to fine growth of pubic hair. Descent of the testicles occurred in only one case. Six patients received antuitrin-S; two, anterior pituitary extract, and six, both extracts.

In one 10 year old boy without cryptorchidism but with hypoplasia of the genitalia and a feminine body build who received 5,566 rat units of both extracts a moderate growth of coarse pubic hair developed without any other change.

From these findings it can be seen that the gonadotropic extracts can produce some of the changes that are associated with developing puberty, but whether these changes will remain stationary, progress or disappear, only further observation will determine.

EFFECT ON THE BEHAVIOR OF PATIENTS

Besides our own observation of each child, we attempted to obtain the mother's observations as to changes in behavior and reactions during the period of treatment. In interpreting these observations one must take into consideration that these children were conscious that more than normal attention was being paid to the genitalia, owing to the frequent examinations. Also the mothers were anxious to have the treatment succeed so that an operation might possibly be avoided.

We thought that thirteen of the seventy-eight patients showed some changes in behavior. A 6 year old boy (case 45) while receiving 11,000 rat units of antuitrin-S showed marked enlargement of the penis. His mother noticed that he was having erection most of the time and that he was masturbating a great deal. The teacher complained of his continual masturbation during school hours. Although he seemed listless, his appetite increased during the period of treatment. During the six months since treatment has been discontinued the penis has decreased

in size but is still considerably larger than normal, and he is reported to have stopped masturbating. While under treatment with antuitrin-S a 2 year old boy (case 47) showed marked enlargement of the penis, with frequent erections. On numerous occasions he was noticed to approach and follow some little girl, patting her on the buttocks and trying to insert his finger into her rectum. He was also observed on several occasions trying to insert objects into his own rectum. Six months after treatment was discontinued the penis had returned to normal size, and the aforementioned practices had apparently stopped. A 6 year old boy (case 68) who had always been shy, never making advances to any one in the clinic, during the course of treatment on several occasions approached the volunteer writer in the examining room and kissed her, a marked change from his normal behavior.

The reaction of a mother and her 13 year old boy (case 10) is undoubtedly of no significance. Extensive medical treatment for bilateral cryptorchidism was not effective, so the testicles were operated on with excellent results. The mother informed us before treatment that she had planned to have the boy become a priest, but after the successful operations she said she had decided to make other plans for him.

A 9 year old boy (case 22) began picking fights frequently with other children, a 5 year old boy (case 20) became much harder for the mother to handle and a 10 year old boy (case 59), according to the mother, was becoming mischievous. An 11 year old boy (case 64) while receiving 5 or 6 cc. of anterior pituitary extract three times a week became listless and tired. When treatment was stopped he felt much better and became more active. This was also true of a 2 year old boy. Four boys (cases 17, 18, 57 and 69) became more alert and active and ate much better during treatment. Two of these boys, one obese and one a cretin, received thyroid, which would undoubtedly explain the feeling of well-being.

EFFECT ON THE CARPAL BONES

Roentgenograms were taken of the wrists of all patients before treatment was started. They were all found to be normal, except in one boy, a cretin, who showed a decreased number of ossification centers. Follow-up roentgenograms after treatment was terminated have been made for only ten patients. None of these showed any change from the normal. Further roentgenograms are to be made for the whole series of patients.

EFFECT ON THE URINE

The urine was examined weekly during the course of treatment. In no instance was there any change from the normal. Glycosuria, which has been occasionally reported by others, was never encountered.

REACTIONS FROM INJECTIONS

One or more local or general reactions from the gonadotropic extracts occurred in each of thirty-two patients. In eleven there was, after the first few doses, local erythema lasting for several hours at the site of the injection. Antuitrin-S was administered to three of these reactors and anterior pituitary extract to eight. Pain, erythema and induration lasting from three to four weeks occurred at the site of one or more injections in nine boys. Abscess formation never appeared. These reactions were noted less often with antuitrin-S than with anterior pituitary extract but about equally often for the subcutaneous and the intramuscular injections.

Twelve patients (eight receiving antuitrin-S and four anterior pituitary extract) complained of pain in the groin or that the testicle became sensitive after some of the injections. This discomfort sometimes lasted for several days. Four boys after receiving the larger doses of anterior pituitary extract complained of malaise and aching. Nausea or vomiting lasting several hours occurred in four boys after some of the injections of both extracts.

Acute abdominal pain lasting for several hours after each of two injections of antuitrin-S occurred in two boys. In one the testicle was not palpable, while in the other the testicle was in the canal. What was interpreted as torsion of the testicle in the inguinal canal occurred once. This seemed to correct itself, with no change in the size of the testicle afterward. Dysuria lasted for several days in one boy receiving antuitrin-S. In one boy painful swelling of the breast occurred and lasted several days.

Twice when a large dose of antuitrin-S was administered to one boy a rash developed that was similar to pityriasis rosea. This never occurred when he was receiving smaller doses. One patient had a severe allergic reaction, as manifested by urticaria, coughing, sneezing and dyspnea from fifteen to twenty minutes after receiving 1 cc. of anterior pituitary extract on three consecutive occasions. This child had no reaction from antuitrin-S. Another patient had a nodular swelling of the parotid gland while under treatment. It subsided after several days and was not thought to be due to mumps.

The aforementioned reactions occurred in patients between the ages of 2 and 13 years. No type of body build seemed a predisposing factor, and the two extracts were responsible for about an equal number. In twenty-three of the reactors subcutaneous injections were used and in nine intramuscular injections. There seemed to be only a rare direct relationship between the size of the individual dose and the reaction, except that toxic manifestations seemed to occur more frequently after the large injections, of 4 or 5 cc.

POSSIBLE HAZARDS OF TREATMENT

It will undoubtedly require several years of observation of these patients before it is possible to be absolutely sure of all the effects of this type of therapy. There was no evidence of atrophy of the genitalia during the period of active treatment or during the later period of observation. If a testicle was hypoplastic before treatment, further atrophy did not take place, nor did it take place after enlargement of a normal-sized testicle. It seemed that at times when a testicle became larger and firmer during treatment, it would later become smaller and softer than normal for a period and then would return to normal.

We are still concerned over the marked enlargement of the penis that occurred in several boys 6 years of age or younger. While two have returned to normal size, six are still considerably larger than normal. Just what the final outcome will be no one can state, but it seems from the fact that no other genital or hormonal changes are evident that no harm has been done.

The behavior and psychologic effects as they relate to sex and masturbation have seemed to correct themselves. No unfavorable effects on the height or weight or on the carpal bones have been noted.

Just what influence there has been on the development of puberty cannot be stated. While in several young boys there has been a decided growth of pubic hair no other associated pubertal changes have occurred in them. The boys that showed more of the changes associated with puberty were all of the age when these changes can be expected to take place. One must also wonder whether all the testicular function of the adult will develop and be maintained in these children who have had genital stimulation and enlargement while young.

OBSERVATIONS AT OPERATION ON UNSUCCESSFULLY TREATED PATIENTS

After unsuccessful treatment with the gonadotropic extracts twenty-two of the cryptorchid patients were operated on. In sixteen patients normal-sized testicles were present, two intra-abdominal and fourteen in the inguinal canal. In two the testicles were smaller than normal, and in four they were so small as to be considered atrophic; all were in the inguinal canal.

Sufficient adhesions to hold the testicle in the inguinal canal were noted in only eight patients. The testicles of these patients were of normal size in six, atrophic in one, and smaller than normal in one. A small inguinal hernia was observed at operation in thirteen patients.

The operative result was considered excellent in fourteen patients because of a normal-sized testicle in the scrotum. The four atrophied

testicles continued to be atrophic. One operative result was considered fair; two were considered poor because the testicles did not remain completely in the scrotum and some decrease in size occurred. One patient was not reexamined. Not including the patients with atrophic testicles, the results of treatment with gonadotropic extracts followed by operation were excellent in 82 per cent of the patients treated.

CONCLUSIONS

From a study of seventy-one boys with ninety-one undescended testicles who were given injections of the gonadotropic principle of the urine of pregnant women (antuitrin-S) and the gonadotropic principle of the anterior lobe of the pituitary gland, it is found that these extracts produce changes in the external genitalia of some patients but not in all.

These changes when present are manifested by flushing of the genitalia, by enlargement of the testicles and penis or by descent of the testicles.

In the patients treated with antuitrin-S 48 per cent of the undescended testicles completely descended into the scrotum by the end of treatment, but only 45 per cent remained descended. If the partially descended testicles are included then 61 per cent can be considered benefited.

In the patients treated with the gonadotropic principle of the anterior lobe of the pituitary gland 25 per cent of the testicles completely descended into the scrotum, but only 18 per cent remained descended. Including those in whom the testicles partially descended 35 per cent were benefited.

When both gonadotropic extracts were used in treating the patient, 40 per cent of the cryptorchid testicles showed complete descent, but only 25 per cent of the testicles remained in the scrotum; 55 per cent were benefited.

The obtaining of better results with the gonadotropic principle of the urine of pregnant women is probably due to the greater number of rat units administered.

When descent of the testicle occurs, it usually begins to take place before 4,000 rat units of the gonadotropic principle have been administered.

Treatment seems to be about equally successful at any age after the first year, but owing to other changes which may take place it seems better not to begin treatment until after the seventh year of age.

The size of the individual dose and the total rat units administered seem to bear no relation to the age of the patient in producing descent of the testicles.

In a control series of fourteen untreated and inadequately treated patients (seventeen undescended testicles) descent of the testicles did not occur.

Both extracts often caused enlargement of small testicles but never permanent enlargement of normal-sized testicles.

Both extracts produced enlargement of a normal-sized penis in eight boys.

No atrophy of any part of the external genitalia has been observed as a result of treatment.

Reactions both general and local may occur during treatment.

Treatment had no effect on weight or height or on body build, even when hypoplasia of the genitalia was present, with a feminine type of body build.

The observations at operation on twenty-two patients with cryptorchidism unsuccessfully treated with the gonadotropic extracts are reported.

The gonadotropic factor of the urine of pregnant women should be given a fair trial in the treatment of cryptorchidism of boys over 7 years of age. If improvement does not occur by the time about 4,000 rat units has been administered, operation may be considered.

MENTAL GROWTH OF EPILEPTIC CHILDREN

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Whatever the intellectual endowment of an epileptic child, his mental growth is retarded more often than it is accelerated. This clinical dictum raises several questions regarding the mechanism of the disease which are significant in developmental supervision. 1. Does mental deterioration form a part of epilepsy? 2. Does the initial intelligence determine the alteration in the mental state? 3. Does reduction in the number of seizures raise the mental capacity? 4. Does improvement in the epileptic condition enhance mental control? 5. Does the age condition the change in mental status? The answers were tentatively obtained from clinical and psychologic studies of 129 epileptic children selected from about 1,700 institutionalized children, and of 91 children from private practice who were studied in hospitals and special schools.

DISTRIBUTION OF CASES

The diagnosis of epilepsy was derived from detailed physical, neurologic and psychologic examinations of the patient. It was based on the medical and personal history, mental tests, analysis of blood and spinal fluid, determinations of the basal metabolic rate, roentgen examination of the skull and gastro-intestinal tract, tests for allergy and ventriculography as indicated.

In this study the following conditions were fulfilled: (1) Reliable psychological examinations were given at the beginning and at the end of the interval of study; (2) there were no complications affecting the mental status; (3) mental levels were over an intelligence quotient of 20; (4) therapeutic procedures were uniform, and (5) living conditions were identical.

The condition was classified as primary if idiopathic epilepsy was the sole disturbance and as secondary if, besides epilepsy, a constant cerebrogenic factor was superimposed on the mental status. In patients with the former type mental growth might be expected to be accelerated, and in those with the latter, to be retarded. The children were

From the New York City Children's Hospital.

considered to be improving if both the number and the intensity of the seizures decreased and to be unimproved if the number of attacks increased and the intensity decreased and vice versa, or if there was no change in the condition during the interval of study.

The treatment was formulated according to individual needs. For the children with an intelligence quotient of less than 90, it consisted of administration of phenobarbital, limitation of fluid and salt, regulation of the bowels and daily periods of rest. For the children with an intelligence quotient of more than 90, treatment consisted of a keto-

TABLE 1.—*Distribution of Epileptic Children Studied*

Classification				
	Improved		Unimproved (Treated and Untreated)	
Epilepsy	Hospital	Private	Hospital	Private
Primary	32	56	55	35
Secondary	24	..	18	..

Chronological Ages						
	Improved			Unimproved (Treated and Untreated)		
	Hospital		Private	Hospital		Private
Frequency	Primary	Secondary	Primary	Primary	Secondary	Primary
Median	9 yr. 6 mo.	14 yr.	7 yr. 9 mo.	13 yr. 2 mo.	12 yr. 8 mo.	8 yr. 5 mo.
25%	6 yr.	7 yr.	4 yr. 6 mo.	8 yr. 9 mo.	6 yr. 6 mo.	6 yr. 8 mo.
75%	14 yr. 6 mo.	20 yr.	10 yr. 9 mo.	18 yr. 3 mo.	17 yr. 6 mo.	12 yr.

TABLE 2.—*Age at Onset of Epilepsy*

	Improved			Unimproved (Treated and Untreated)		
	Hospital		Private	Hospital		Private
Frequency	Primary	Secondary	Primary	Primary	Secondary	Primary
Range	1-15 yr.	1-17 yr.	1-14 yr.	1-13 yr.	1-13 yr.	1-13 yr.
Median	3 yr. 6 mo.	2 yr. 6 mo.	3 yr. 3 mo.	2 yr. 10 mo.	2 yr. 8 mo.	3 yr.
25%	1 yr. 5 mo.	8 mo.	1 yr.	9 mo.	1 yr. 9 mo.	1 yr.
75%	11 yr. 11 mo.	11 yr. 9 mo.	8 yr.	6 yr. 7 mo.	10 yr. 6 mo.	8 yr. 8 mo.

genic diet, acid-forming and dehydrating, administration of phenobarbital, removal of physical and mental strains, elimination of allergic offense, change of environment, correction of physical defects, faulty posture and constipation, periods of rest before and after meals and a regulated daily regimen.

AGE AT ONSET OF EPILEPSY

Exact determination of the beginning of epilepsy is frequently difficult because no adequate method of distinguishing epileptic seizures from the nonepileptic convulsions of infancy and early childhood has

been devised. The general trend of the data was significant, in that in most of the cases studied the seizures began in the preschool period. The age of onset of seizures in the patients with primary epilepsy who showed improvement was slightly higher than in the unimproved group, but the greater variability in the improved group offset this difference. With a few outstanding cases omitted, the age of onset of convulsions ranged from birth to 15 years, with the 25 percentile at about 1 year, the 50 percentile at about 3 years and the 75 percentile below 12 years. The similarity in these distributions indicated that the age of onset does not condition the mental status of the epileptic child.

DETERMINATIONS OF THE INTELLIGENCE QUOTIENT

The constancy of relative mental ability is most commonly expressed by the intelligence ratio. Terman, Rugg, Garrison and others have shown surprisingly constant relative abilities of children tested year

TABLE 3.—*The Intelligence Quotients of Epileptic Children*

	Improved			Unimproved (Treated and Untreated)		
	Hospital			Hospital		
Frequency	Primary	Secondary	Private Primary	Primary	Secondary	Private Primary
Range.....	20-84	20-74	40-140	20-88	20-85	40-140
Median.....	56	51	99	49	49	90
25%.....	46	40	67	41	41	54
75%.....	64	59	106	66	57	100

after year under normal conditions. Hence the increase in mental age of a child which is expected after a given interval will depend partly on the length of this interval and partly on the intelligence quotient. The mental age of a child whose intelligence quotient is 100 will in twelve months increase 100 per cent, whereas that of a child with an intelligence quotient of 50 will in the same time increase only 50 per cent, the six months' increase of a normal child. The ratio of the actual increase to this expected increase gives a measure of the stability of intelligence. If the rate is 1, mental development is normal; if less than 1, development is retarded; if 0, development is stagnant. This involves two assumptions: that the units of the score are equal at all levels of the test, which is doubtful, and that the selection of children at each age is the same, which is also doubtful. Nevertheless we resorted to mental tests as the best approach to our problem.

The initial and final tests used in the mental studies of epileptic children involved a variety of scales. The final rating was a weighed average of appropriate measures. The Stanford-Binet test was supplemented by the Pintner-Paterson test for performance, the Kelley-Traube test for language completion, the Parteus maze test or the Pintner

nonlanguage test. Not all the scales were used in each case, for the choice depended on the clinical needs of the individual patient. The Kuhlmann-Binet test was substituted for the Stanford-Binet test in most cases of children below the age of 5 years. Scales requiring the use of language were omitted when the child had a marked defect in speech or a background of a foreign language. The intelligence quotients of children 15 years of age or over were determined by dividing the mental age by 180 months, as 15 years is the accepted level of maturity.

The hospitalized epileptic children were retarded mentally. The mental status of these selected children was in accord with that recorded for institutional epileptic patients.[1] No significant mental difference between primary and secondary types of epilepsy appeared in these children. Children with epilepsy of both types were within the mental range of the unselected mentally retarded children in the hospital. But there was some difference in intelligence quotient in favor of the improved group of children as compared with the unimproved, treated or untreated.

The group of epileptic children from private practice showed a normal mental rating significantly higher in the improved than in the unimproved patients. It corresponded well with the central tendency and total range of the mental rating of other pediatric patients. Other observers [2] recorded slightly lower intelligence quotients for the mentally normal epileptic children. On the other hand, we have seen many epileptic children display superior intelligence when tested early in the course of the disease, especially those who have had only attacks of petit mal. Apparently the large number of mentally retarded epileptic patients observed in the institutional group is statistically balanced by a greater number of patients with more than average intelligence in the group from private practice. The selected nature of the groups studied by various investigators, however, precludes strict comparisons.

MENTAL GROWTH

The changes in intelligence quotient were determined by retests for each group of children, those institutionalized and those treated in private practice. The conditions of the tests were favorable to the best response. No data were recorded for children under the immediate

1. Fox, J. T.: Brit. J. M. Psychol. **4**:235, 1924. Annual Report of the New York State Department of Mental Hygiene, Albany, J. B. Lyon Company, 1930-1933. Fetterman, J., and Barnes, M. R.: Serial Studies of Intelligence of Patients with Epilepsy, Arch. Neurol. & Psychiat. **32**:797 (Oct.) 1934.

2. Sullivan, E. B., and Gahagan, L.: On the Intelligence of Epileptic Children, Genetic Psychology Monograph, no. 5, Worcester, Mass., Clark University Press, 1935, vol. 17, p. 330.

influence of seizures. The retests therefore indicated the effects of the disease, treated or untreated, on mental status. The intervals between the initial and the final test varied from three months to three years, but the results are valid for comparison since the correlation with interval change was negligible ($+ 0.105 \pm 0.12$). But the correlation between the first and the final test was $+ 0.90$.

The histograms [3] and table 4 reveal a constant difference between the improved and the unimproved group, irrespective of the initial intelligence quotient, at the lower end of the distribution. This indicates that whereas both improved and unimproved children were limited alike in their ability to raise their mental status, the unimproved as a group dropped twice as low at the 75 percentile of the distribution.

TABLE 4.—*Changes in the Intelligence Quotients of Epileptic Children*

	Improved			Unimproved (Treated and Untreated)		
	Hospital			Hospital		
Frequency	Primary	Secondary	Private Primary	Primary	Secondary	Private Primary
Range.....	+15 - —22	+14 - —15	+21 - —21	+9 - —44	+7 - —47	+3 - —42
Median.....	—2	0	—0.5	— 3	— 3	— 5
25%.....	—6	—6	—5	—12	—13	—12
75%.....	+2	+1	+3.7	0	— 2	0

TABLE 5.—*Correlations*

Factors		Cases (Primary)	Correlation
Chronological age	I. Q. changes	87	$+0.215 \pm 0.07$
Initial I. Q.	I. Q. changes	87	-0.286 ± 0.07
Chronological age	Initial I. Q.	87	-0.144 ± 0.08
Testing intervals	I. Q. changes	32	$+0.105 \pm 0.12$
Testing intervals	I. Q. changes	55	$+0.127 \pm 0.07$

Mental deterioration was thus prevented by treatment in both the institutional group and that taken from private practice. The histograms of the two improved groups show no tendency to a large drop at the lower end of the distribution. Mental deterioration in the unimproved group appeared to be augmented by the severity, frequency, early onset and duration of the attacks.

The epileptic children cured of their seizures showed constancy of the intelligence quotient, with less variability than the other groups.

3. The histogram is a convenient method of representing the frequency distribution of the data. The assumption is made that all of the scores within an interval of abscissas are spread uniformly over the entire interval. For this reason, the measures are represented by a rectangle constructed with a base equal to the length of the abscissa and an altitude equal to the number of measures within the interval. The total frequency is represented by the area of the histogram, and the area of each rectangle is directly proportional to the number of measures in the interval.

But the difference might disappear if the number of cases studied were increased. Again, any difference of less than 5 in the intelligence quotient is within the probable error or natural variability of the intelligence quotient itself and is therefore not highly significant.

Brighter subjects showed a slight tendency to greater deterioration ($r = -0.286 \pm 0.07$). The younger children, however, were some-

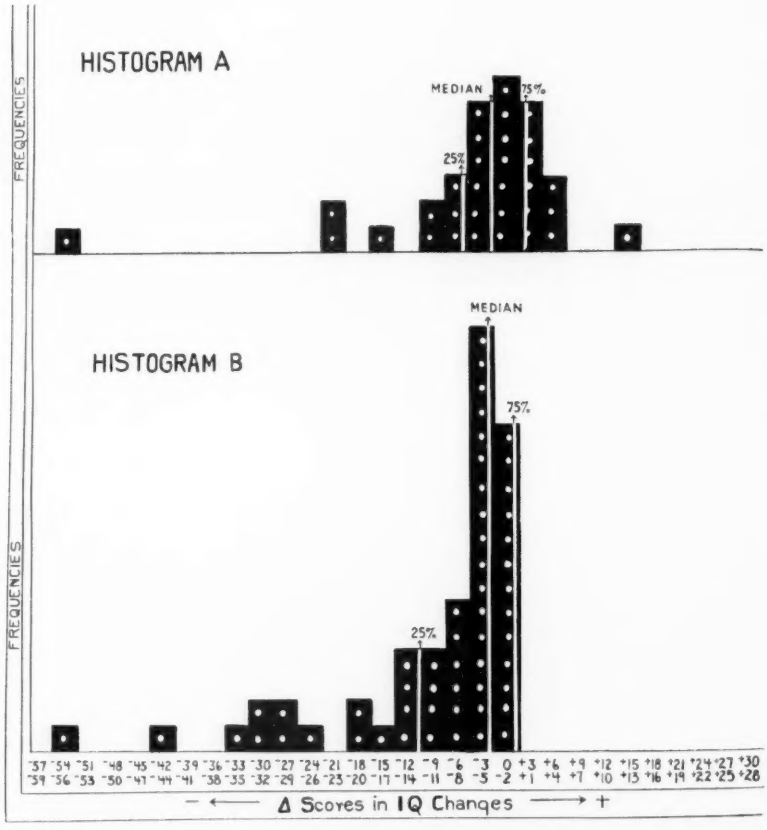

Chart 1.—Histogram *A* shows changes in intelligence quotient on retests of improved epileptic patients with a rating of less than 90 (median = —2; 25 per cent = —6; 75 per cent = + 2). *B* shows changes in intelligence quotient of unimproved epileptic patients, treated and untreated, with a rating of less than 90 (median = —3; 25 per cent = —12; 75 per cent = 0).

what brighter than the older ones ($r = -0.144 \pm 0.08$); hence the rise in intelligence quotient cannot be ascribed to age alone. This factor is further complicated by the greater variability shown by nonepileptic children of higher and lower levels of intelligence. The differences in

the various groups shown by the first rating of intelligence are too small to indicate advantage to any group—improved or unimproved, primary or secondary.

Younger patients responded to treatment more favorably than older children. And the earlier it was instituted, the greater its effectiveness. Nevertheless, the degree of favorable change in mental status was

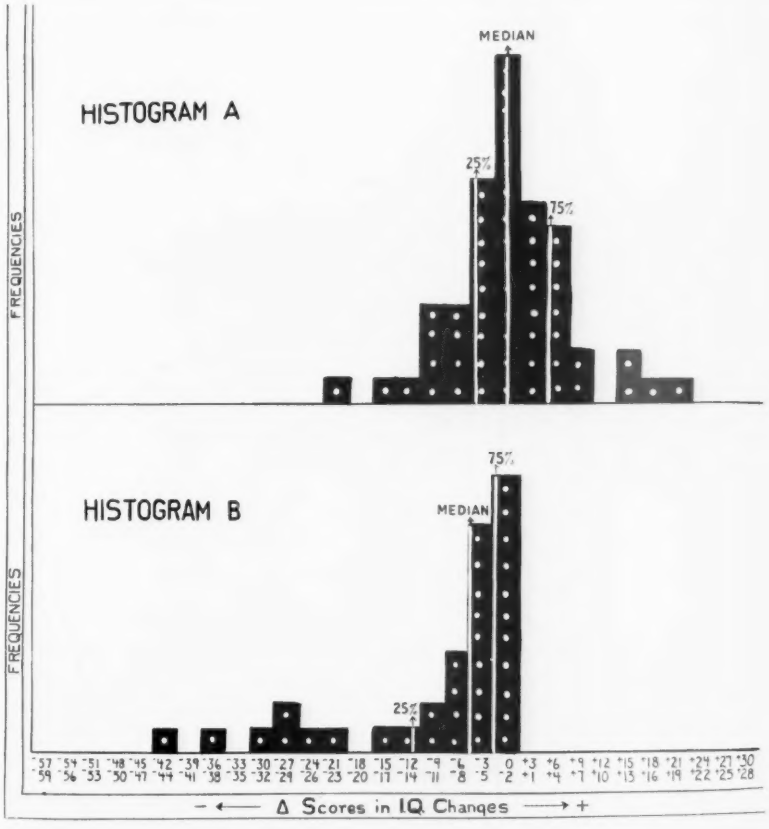

Chart 2.—Histogram *A* shows changes in intelligence quotient of improved epileptic patients with a rating of more than 90 (median = —0.5; 25 per cent = —5; 75 per cent = + 3.7). *B* shows changes in intelligence quotient of unimproved epileptic patients, treated and untreated, with a rating of more than 90 (median = —6; 25 per cent = —12; 75 per cent = —1).

slightly greater in the older subjects. The correlation r = + 0.215 ± 0.07 is, however, too low to have great significance.

Our groups did not show the degree of deterioration observed by others.[4] And the improved groups at any level of intelligence showed

4. Patterson, H. A., and Fonner, D.: Psychiatric Quart. **2**:542, 1928. Dawson, S., and Conn, J. C. M.: Arch. Dis. Childhood **4**:142, 1929.

the minimal, if any, mental deterioration. Despite the differences in the treatment given the two groups, the children whose seizures were diminished or arrested showed normal mental growth. The predominance of drug therapy in the institutional cases and of dietary therapy in the private cases did not alter the mental status on improvement. Apparently, epileptic children, irrespective of their mental endowment, deteriorate mentally with the progress of the disease if unimproved by treatment.

MENTAL CONTROL

The changes in mental control were evaluated from clinical judgments of behavior. The emotional and nervous stability of relations formed in the ward and in school were considered. The percentages thus derived showed no significant differences in the two groups. Life is difficult for these children. Much behavior that is attributed to underlying temperament can be assigned to chronic invalidism. Mental sluggishness may be the outcome of treatment with drugs and a nar-

TABLE 6.—*Mental Control in Epileptic Children*

Changes	Improved		Unimproved (Treated and Untreated)	
	Primary	Secondary	Primary	Secondary
Better	22%	21%	15%	22%
Same	41%	58%	47%	45%
Worse	37%	21%	38%	33%

rowed horizon of activity, and emotional imbalance, a consequence of unrealizable aims. Many rise superior to their inferiority, do their school work, never enter institutions and betray no sign of affective instability or intellectual deficiency.

SUMMARY

Clinical and psychologic studies were made of 129 epileptic children selected from about 1,700 institutionalized children and of 91 children from private practice selected from hospitals and special schools. The condition was classified as primary if idiopathic epilepsy was the sole disturbance and as secondary if, besides epilepsy, a constant cerebrogenic factor was superimposed on the mental status. The children were considered improved if either or both the number and the intensity of the seizures diminished and unimproved if either or both the number and the intensity of the attacks did not diminish because of treatment or nontreatment. The mental tests involved a variety of appropriate scales, a weighed average of all results constituting the final rating for each child.

The institutionalized group of epileptic children were retarded mentally but remained within the mental range of the hospitalized unselected children. The group of epileptic children from private practice showed a mental rating significantly higher in the improved than in the unimproved patients. The large number of mentally retarded epileptic children observed in the institutionalized group were statistically balanced by a greater number of children of more than average intelligence in the group from private practice.

Histograms of retests revealed a constant difference between the improved and the unimproved group, irrespective of the initial intelligence quotient. The unimproved group dropped twice as low at the 75 percentile and showed a large drop at the lower end of the distribution. Mental deterioration was thus prevented by treatment in both institutionalized patients and those from private practice. The changes in mental control within various intervals showed no significant difference between the two groups.

INFLUENCE OF LETHARGIC ENCEPHALITIS ON INTELLIGENCE OF CHILDREN

AS DETERMINED BY OBJECTIVE TESTS

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It is generally recognized that an acute attack of lethargic encephalitis in a child frequently produces marked disturbances in personality and behavior. There is, however, disagreement in regard to the influence of the disease on general intelligence. The study reported here was an attempt to determine by quantitative measurements the change in general intelligence of children afflicted with the disease.

There have been reported instances of feeblemindedness which appeared directly attributable to the disease.

Paterson and Spence [1] (1921) reported a "state of permanent and hopeless idiocy" existing in seven of a group of twenty-five children who before acquiring the disease were of "normal health and intelligence."

Ebaugh [2] (1923) reported the case of a child who at the age of 6 years had a mental age of 2 years, the age at which she acquired the disease. Previous to that age she had "showed normal mental development."

Da Fano and Ingleby [3] (1924) described a "bodily and mentally well developed female child, with healthy antecedents" who showed a mental condition which "resembled idiocy" within a year after acquiring the disease at the age of 1 year and 8 months. "Histopathological investigations revealed the presence of changes essentially similar to those seen in subacute cases of epidemic encephalitis but characterized by an unprecedented severity and diffusion to all cerebral regions."

Bromberg [4] (1930) reported the case of a boy "whose birth and early development presented no physical or mental abnormality" and whose "family history

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Studies from the Institute for Juvenile Research, 907 South Lincoln Street, Chicago, Paul L. Schroeder, M.D., Director, Series C, No. 281.

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2. Ebaugh, F. G.: Neuropsychiatric Sequelae of Acute Epidemic Encephalitis in Children, Am. J. Dis. Child. **25**:89 (Feb.) 1923.

3. Da Fano, C., and Ingleby, H.: Histopathological Observations in an Unsuspected Case of Chronic Epidemic Encephalitis in a Young Child, J. Path. & Bact. **27**:349 (Oct.) 1924.

4. Bromberg, W.: Mental States in Chronic Encephalitis, Psychiatric Quart. **4**:537 (Oct.) 1930.

was negative," who at the age of 11 years had a mental age of 6.8 years, after an acute attack of the disease at the age of 3 years.

In various series of cases for which results of objective tests of intelligence have been reported, initial intelligence ratings subsequent to the onset of the disease have been found to fall below the ratings of normal children.

Robin[5] (1923) reported results of the Binet test for a series of eleven subjects whose chronological ages ranged from 7 to 13 years, with a mean of 9.1 years. The range of intelligence was from the imbecile level to the average, the median intelligence quotient being 81.

Sherman and Beverly[6] (1923) reported results of the Terman-Binet test for a series of twenty subjects whose chronological ages ranged from 3 to 19 years, with a mean of 12.4 years. The range of intelligence was from the high grade defective level to the very superior, the mean intelligence quotient being 88 ± 1.9.

Hallowell[7] (1925) reported results of the Terman-Binet test for a series of twenty-one subjects whose chronological ages ranged from 6 to 19 years, with a mean of 11.1 years. The range of intelligence was from the high grade defective level to the average, the mean intelligence quotient being 88 ± 1.77.

Kwint[8] (1926) reported results of the Binet test for a series of thirteen subjects whose chronological ages ranged from 8 years to 12 years. The range of intelligence was from the borderline defective level to the superior, the median intelligence quotient being 91.

Shrubsall[9] (1927) reported results of the Binet test for a series of twenty-one subjects whose chronological ages ranged from 5 to 14 years, with a mean of 9.8 years. The range of intelligence was from the high grade defective level to the average, the mean intelligence quotient (approximate) being 82 ± 2.23.

Lange[10] (1928) reported results of the Bobertag-Binet test for a series of thirty-nine subjects whose chronological ages ranged from 8 to 15 years, with a mean of 11.5 years. The range of intelligence was from the high grade defective level to the average, the mean intelligence quotient being 83 ± 1.32.

Bromberg[4] (1930) reported results of the Terman-Binet test for a series of fifteen subjects whose chronological ages ranged from 9 to 21 years. The range of intelligence was from the high grade defective level to the average, the mean intelligence quotient being 73.

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5. Robin, G.: Considérations sur les troubles mentaux liés aux formes prolongées de l'encéphalite épidémique chez l'enfant, Thése de Paris, no. 380, 1923.

6. Sherman, M., and Beverly, B. I.: The Factor of Deterioration in Children Showing Behavior Difficulties After Epidemic Encephalitis, Arch. Neurol. & Psychiat. **10**:329 (Sept.) 1923.

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8. Kwint, L.: Beiträge zur Klinik und Pathogenese der Folgeerscheinungen von epidemischer Encephalitis bei Kindern, Ztschr. f. Kinderh. **40**:678 (Feb.) 1926.

9. Shrubsall, F. C.: The Sequelae of Encephalitis Lethargica, Brit. J. M. Psychol. **7**:210 (July) 1927.

10. Lange, W.: Die Entwicklung der Intelligenz bei Kindern nach Encephalitis epidemica, Psychiat.-neurol. Wchnschr. **30**:579 (Dec. 15) 1928.

Scott[11] (1930) reported results of the Terman-Binet test for a series of thirty-five subjects whose chronological ages ranged from 3 to 24 years, with a mean of 11.9 years. The range of intelligence was from the high grade defective level to the very superior, the mean intelligence quotient being 88 ± 1.71.

Bond and Appel[12] (1931) reported results of the Terman-Binet test for a series of forty-eight subjects whose chronological ages ranged from 6 to 14 years, with a mean of 9.7 years. The range of intelligence was from the high grade defective level to the superior, the mean intelligence quotient being 85 ± 1.37.

Dawson and Conn[13] (1931) reported results of the Burt-Binet test for a series of fifty subjects whose chronological ages ranged from 3 to 13 years, with a mean of 8.4 years. The range of intelligence was from the high grade defective level to the superior, the mean intelligence quotient being 85 ± 1.23. (Comparisons revealed significant differences between the ratings of the encephalitic children and those of their normal siblings and of nonencephalitic patients, respectively, in favor of the controls.)

Berrien[14] (1934) reported results of the Terman-Binet test for a series of twenty-four subjects whose mean chronological age was 14.3 years. The ratio of the obtained difference between the chronological age and the mental age to the standard deviation of that difference was 5.3.

Jenkins and Ackerson[15] (1934) reported results of the Terman-Binet test for a series of fifty-seven subjects whose chronological ages ranged from 5 to 29 years, with a mean of 13.6 years. The range of intelligence was from the idiot level to the very superior, the mean intelligence quotient being 75.

Comparisons of successive intelligence ratings subsequent to the onset of the disease have disclosed different trends.

1. In certain series a progressive retardation of intelligence was found.

Shrubsall[9] reported results of retesting for a series of twenty-one subjects with a mean difference in intelligence quotient (last minus first) of — 11.19 ± 1.78.

Lange[16] reported results of retesting for a series of twenty subjects with a mean difference in intelligence quotient (last minus first) of — 7.85 ± 1.46.

Dawson and Conn[13] reported results of retesting for a series of fifty subjects with a mean difference in intelligence quotient (last minus first) of — 13.46 ± 1.05.

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11. Scott, L. M.: The Role of the Psychiatric Social Worker in the Treatment of Post-Encephalitis, Smith College Studies in Social Work, 1930, p. 180.

12. Bond, E. D., and Appel, K. E.: The Treatment of Behavior Disorders Following Epidemic Encephalitis, New York, The Commonwealth Fund, Division of Publications, 1931.

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15. Jenkins, R. L., and Ackerson, L.: The Behavior of Encephalitic Children, Am. J. Orthopsychiat. **4**:499 (Oct.) 1934.

16. Lange,[10] Lange, W.: Erfahrungen und Ergebnisse auf Grund einer zehnjährigen Beobachtung in der Enzephalitiker-Abteilung Chemnitz-Altendorf, Ztschr. f. Kinderforsch. **43**:263 (Nov.) 1934.

(The rate of development in intelligence for the encephalitic child was computed to be less than half that for the normal child.)

2. In other series no appreciable change in intelligence was found.

Scott [11] reported results of retesting for a series of twenty-nine subjects with a mean difference in intelligence quotient (last minus first) of — 2.0 ± 1.40.

Jenkins and Ackerson [15] reported results of retesting for a series of twenty-one subjects with a mean difference in intelligence quotient (last minus first) of —2.3 ± 1.10.

3. On the other hand, in certain series acceleration of mental growth was found to occur.

Sherman and Beverly [6] reported results of retesting for a series of sixteen subjects with a mean difference in intelligence quotient (last minus first) of + 5.06 ± 1.06.

Bond and Appel [12] reported results of retesting for a series of fifteen subjects with a mean difference in intelligence quotient (last minus first) of + 8.2 ± 1.12.

The study reported here was a further attempt to ascertain by quantitative measurement the effect of the disease on the general intelligence [17] of children.

SELECTION OF CASES

The cases for this study were selected chiefly from the files of the Institute for Juvenile Research. Some were obtained from the state schools for the feeble-minded at Lincoln and Dixon, Ill. A few were obtained from Kings Park State Hospital, Kings Park, N. Y., and from the Spaulding School for Crippled Children in Chicago.

Those cases in which the history or physical examination gave any indication of encephalitis or "sleeping sickness" and in which two or more ratings on the Stanford-Binet intelligence test were available were selected from the files. The records from the Illinois institutions were carefully reviewed by one of us (Jenkins) for the purpose of excluding all cases in which the diagnosis was doubtful. Only those cases in which the diagnosis of lethargic encephalitis could be considered established or well supported were retained. The hospital's diagnosis was accepted for the cases from Kings Park State Hospital.

The cases of 108 subjects who were finally selected (as having or having had lethargic encephalitis) were again reviewed (by Jenkins) and divided into two groups: those in which there appeared fairly pronounced signs of parkinsonism and those in which there did not. There were 40 cases in the former group and 68 in the latter. The records were again reviewed and the cases again divided into two groups: those in which there were gross disturbances of personality and behavior (which were characteristic of lethargic encephalitis and for which other explanations were not apparent) and those in which there appeared no such disturbances. The cases were also divided into three groups, according to the age of the child at the onset of the acute phase of the disease.

17. In this study intelligence is defined in terms of performance on the Stanford-Binet Intelligence Test.

PRESENTATION OF RAW DATA

The raw data on the 108 cases are given in table 1, the first column of which gives the number of the case and the second the sex of the patient. In the third column, *P* indicates that there appeared fairly pronounced signs of parkinsonism and *NP* indicates that no signs of parkinsonism were observed; in the fourth column, *B* indicates that there were marked changes in the personality and behavior and *NB* indicates that no such changes were present, while a blank space indicates that no data regarding behavior were available; the fifth column gives the age at the time of the onset of the disease, as nearly as could be determined from the record; the remaining columns give the chronological age (*C.A.*), the mental age (*M.A.*), the intelligence quotient (*I.Q.*) and the personal constant (*P.C.*) [18] for each of the different examinations. In a few cases there were more than five examinations, and in such instances the last was taken as the fifth.

NATURE OF MENTAL GROWTH

It may be proper at this point to consider some of the difficulties which arise in analyzing these data for the influence of the disease on general intelligence. First of all, there is no agreement in regard to the nature of mental growth for the normal person. When equal units of mental growth are plotted against age, is the resulting curve one of negative acceleration? Is it an ogive? Or is it a straight line angulated at from 14 to 16 years? These questions have not as yet been answered satisfactorily.

It has frequently been assumed that the curve of mental growth is one of negative acceleration—that is, that mental growth is relatively rapid during infancy and early childhood, that it becomes progressively less rapid and that at some age between 15 and 20 years growth ceases entirely. Thorndike and others,[19] using the C. A. V. D. scale, concluded that the curve of mental growth with age "is of the general parabolic form." Pintner [20] has accepted such a curve as best fitting the

18. The personal constant (P.C.) is a measure of brightness which Heinis, Kuhlmann and others have advocated as a substitute for the intelligence quotient (I.Q.). Their contention is that it remains more nearly constant because it is derived from a mental growth curve of negative acceleration. Theoretically, if such a growth curve be assumed, the intelligence quotient must drop for "dull" children. It was for this reason that both measures were used. See: (*a*) Heinis, H.: A Personal Constant, J. Educ. Psychol. **17**:163 (March) 1926. (*b*) Riley, G. L.: A Comparison of the P.C. and I.Q., Psychol. Clin. **18**:261 (Feb.) 1930. (*c*) Cattell, P.: The Heinis Personal Constant as a Substitute for the I.Q., J. Educ. Psychol. **24**:221 (March) 1933. (*d*) Hilden, A. H.: A Comparative Study of the Intelligence Quotient and Heinis' Personal Constant, J. Applied Psychol. **17**:355 (Aug.) 1933. (*e*) Kuhlmann, F.: What the I.Q. Means Today, Nation's Schools **11**:33 (Feb.) 1933. (*f*) Bradway, K. P., and Hoffeditz, E. L.: The Basis for the Personal Constant, J. Educ. Psychol. **28**:501 (Oct.) 1937.

19. Thorndike, E. L., and others: Measurement of Intelligence, New York, Teachers College, Columbia University Press, 1927, p. 463.

20. Pintner, R.: Intelligence Testing, New York, Henry Holt & Company, Inc., 1931, p. 76.

TABLE 1.—*Raw Data*

No.	Sex	Parkinsonism*	Behavior Disorder†	Age of Onset, Yr.	First Test				Second Test				Third Test				Fourth Test				Fifth Test			
					C.A.	M.A.	I.Q.	P.C.	C.A.	M.A.	I.Q.	P.C.	C.A.	M.A.	I.Q.	P.C.	C.A.	M.A.	I.Q.	P.C.	C.A.	M.A.	I.Q.	P.C.
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
1	F	NP	B	5	11-6	8-1	70	85	11-9	8-8	73	88												
2	M	NP	NB	6 mo.	13-1	7-8	59	79	13-9	8-0	58	80												
3	F	NP	B	13	15-11	9-0	60	82	17-1	12-7	83	92	18-11	10-2	68	83	19-7	11-3	75	86				
4	F	P	NB	4	6-2	5-6	89	93	10-0	9-5	94	97	13-10	10-5	75	90	14-3	9-7	67	86	14-11	9-0	60	83
5	M	NP	B	6	8-4	8-9	104	102	11-11	11-0	92	97												
6	M	NP	B	6	12-3	10-6	85	94	14-6	15-6	107	102	15-2	15-7	103	101								
7	M	P	NB	5	11-10	9-0	76	89	15-9	10-10	72	89												
8	M	P	B	5	10-7	8-2	77	89	14-5	8-2	56	80												
9	M	NP	B	7	9-10	7-2	73	85	10-8	6-10	64	80												
10	F	P	B	3	13-7	10-0	73	89	15-3	9-6	63	85	16-3	9-1	60	81								
11	M	P	NB	7	14-4	10-1	70	88	15-0	10-0	66	87												
12	F	NP	B	7	9-9	9-10	101	100	14-0	10-5	74	90	14-5	10-2	70	88	15-1	10-4	69	88				
13	F	P	B	4	16-4	9-1	61	81	17-0	9-1	61	81												
14	M	NP	B	9	10-8	9-1	85	93	11-4	9-4	82	92												
15	M	NP	NB	4	13-5	9-0	67	85	14-2	9-0	63	84												
16	M	NP	NB	8	10-4	9-10	95	98	10-10	9-3	85	93	13-7	13-3	97	99	15-6	13-8	91	97	16-7	13-10	92	95
17	F	P	NB	9	16-8	9-3	62	82	17-4	9-4	62	81												
18	F	NP	B	9	16-9	6-0	40	65	17-5	5-10	39	62												
19	F	NP	NB	3	7-8	7-1	92	96	12-8	9-9	77	90	13-4	9-1	68	86								
20	F	P	NB	3	10-2	6-8	65	81	10-10	7-4	67	83												
21	F	P	...	11	18-5	8-6	56	76	19-1	8-0	53	74												
22	F	P	B	11	18-9	11-0	73	86	19-5	11-0	73	85												
23	M	P	NB	6	8-10	7-0	79	89	14-11	8-10	59	82	15-7	8-0	53	78								
24	F	NP	B	2	9-5	8-1	86	93	9-8	8-6	88	94	10-2	8-0	78	89	11-6	7-8	66	83	12-3	7-10	64	82
25	F	P	B	5	16-2	6-8	44	69	16-10	6-4	42	67												
26	M	NP	B	7	8-6	9-0	106	103	10-2	9-5	92	97	10-11	9-5	86	94								
27	M	NP	NB	5	14-1	8-6	60	82	14-9	7-6	51	76												
28	F	P	...	13	20-4	8-10	59	77	26-1	8-9	58	75												
29	M	NP	B	7	11-6	10-2	88	95	16-1	11-0	73	91	17-8	11-3	75	87								
30	M	P	...	..	7-3	6-7	90	95	9-7	7-7	79	89	11-5	9-6	83	93	12-8	11-5	90	96	14-9	10-9	72	90
31	M	NP	B	10	13-2	7-4	55	77	13-4	7-8	57	79	13-11	7-8	55	78	16-5	7-0	47	71	20-4	6-8	44	66
32	F	NP	B	7	10-10	7-10	72	86	12-1	8-2	67	84	13-0	8-4	64	83	15-3	9-11	66	86	20-6	7-4	49	70
33	M	NP	B	6 mo.	8-7	4-11	57	72	9-11	6-0	60	79												
34	F	P	...	..	26-11	7-0	46	66	28-1	8-4	55	73												
35	F	P	NB	13	24-7	7-6	50	70	26-7	7-4	49	68												
36	M	P	NB	16	18-5	8-10	59	78	25-6	7-0	46	67												
37	M	P	...	..	12-8	7-4	58	78	13-6	7-8	56	79												
38	M	NP	NB	1	4-4	2-10	65	71	5-4	2-10	53	62	6-5	4-0	62	73	8-4	4-8	56	74	10-0	5-2	51	69
39	M	NP	B	3	8-11	7-6	84	92	9-10	7-10	80	86	12-8	8-10	70	86	13-0	8-7	66	84	15-2	10-10	72	89
40	F	P	...	11	13-9	11-1	80	93	14-1	10-5	74	90	14-9	9-7	65	86								
41	F	P	B	9	10-1	8-8	86	93	11-11	8-4	70	86	14-8	9-0	61	83	14-11	8-4	56	80	15-8	8-8	58	80
42	F	P	B	5	17-9	9-0	60	80	20-3	8-9	58	77	22-0	8-10	59	76								
43	F	NP	...	1	8-4	2-10	34	48	8-9	3-0	34	50	11-3	3-4	29	48	13-0	2-8	21	38				
44	M	NP	...	2	8-11	8-5	94	97	10-4	9-0	87	94	11-9	10-1	86	94	13-8	11-10	86	95	14-6	10-7	73	90
45	M	NP	NB	7	9-7	11-3	117	107	12-11	15-2	117	105	13-3	16-4	123	106								
46	M	P	...	..	13-6	7-5	55	77	15-0	8-4	55	80												
47	F	P	...	11	14-5	11-5	79	93	17-10	11-0	73	87	20-2	12-5	82	89	22-6	12-2	81	87	23-6	11-6	77	85
48	F	NP	...	8	9-0	8-8	96	98	10-0	8-4	83	92	12-9	9-10	77	90								
49	F	NP	...	10	13-7	10-7	78	91	17-2	13-9	92	94												
50	M	NP	NB	2	3-0	2-0	67	70	5-1	3-6	69	77	7-0	5-0	72	81	9-1	6-6	72	84	10-1	7-0	69	83
51	M	P	...	5	11-0	6-4	57	76	11-4	7-0	62	80	11-8	6-6	55	75	17-10	6-0	40	64	19-6	6-4	42	65

52	M	P	NB	12	14·6	10·1	69	88	15·0	10·4	69	88	16·0	10·9	72	88	17·5	11·6	77	89	19·1	12·8	84	99
53	M	NP	NB	..	13·8	13·6	99	100	14·1	13·9	98	99												
54	M	NP	...	8	12·11	9·11	77	90	16·2	10·9	72	88	16·3	11·6	77	90								
55	M	P	...	15	16·6	13·10	92	95	17·10	16·0	107	98	19·0	15·7	104	96								
56	M	P	...	..	13·6	10·3	76	90	14·0	8·5	60	82												
57	M	NP	NB	..	11·0	7·11	72	86	15·5	9·7	64	85												
58	F	P	B	..	9·2	6·10	74	86	10·1	5·6	54	72	11·0	6·4	57	76	14·5	6·6	45	70				
59	F	NP	NB	..	9·9	8·9	90	91	12·5	9·9	79	91	14·5	12·1	84	95	15·9	12·4	82	93	20·7	12·6	83	90
60	M	NP	...	1	8·5	6·11	82	90	9·2	7·10	85	93	10·9	7·7	71	85								
61	M	P	B	5	11·11	6·8	56	76	13·8	8·8	63	83												
62	M	NP	...	..	11·5	4·0	35	55	14·4	3·6	24	46												
63	M	P	NB	..	17·3	14·0	93	95	18·7	16·3	108	97	21·4	17·1	114	96								
64	F	NP	NB	5	8·3	6·0	73	84	11·5	5·4	47	67												
65	F	NP	...	7	7·11	3·6	44	59	8·2	3·2	39	54												
66	F	NP	B	12	14·10	9·8	65	86	15·1	10·2	68	87												
67	M	NP	...	..	15·7	14·4	95	98	16·2	17·2	114	101												
68	M	NP	B	9	12·10	10·8	83	93	13·1	9·11	75	90	14·0	11·3	80	93	16·10	11·6	76	89				
69	M	P	NB	9	15·7	10·5	69	87	20·2	11·10	79	87												
70	M	NP	B	10	12·1	9·9	80	92	12·2	8·11	73	88	12·8	9·3	73	88	13·1	9·6	72	88	18·3	8·5	56	77
71	M	P	...	13	15·0	14·8	97	99	17·5	14·2	94	95	18·11	16·0	107	97								
72	F	NP	B	17	22·8	15·4	102	93	24·0	15·7	103	93												
73	M	NP	NB	11	12·2	10·3	84	94	13·3	11·6	86	95												
74	M	NP	B	2	8·8	6·6	75	86	8·11	6·10	76	87	11·7	7·10	67	84	14·1	8·9	62	83				
75	F	NP	NB	14	14·4	12·1	84	95	16·2	11·0	73	89												
76	M	NP	NB	9	11·7	8·10	76	89	14·2	8·10	62	83												
77	F	NP	...	7	7·7	7·2	95	97	9·1	8·0	88	94	11·9	8·10	75	89								
78	M	NP	...	..	8·4	7·4	87	93	10·9	8·2	76	88	11·11	10·6	88	95	13·3	10·2	76	91	15·2	9·7	64	85
79	M	NP	NB	6	10·5	9·4	90	95	14·2	10·3	72	89												
80	F	NP	B	9	12·9	10·6	82	93	14·0	9·8	69	87												
81	M	NP	NB	11	12·4	11·9	95	98	13·3	12·9	96	99												
82	M	P	B	10	17·5	10·9	72	86	18·10	10·3	68	84												
83	F	NP	NB	8	13·10	11·9	85	95	15·8	11·5	76	91	15·11	12·8	84	94								
84	M	P	NB	11	15·5	8·11	59	82	17·3	9·8	64	83												
85	M	NP	...	7	9·7	7·8	80	90	14·5	10·3	71	89												
86	F	NP	NB	4	10·7	10·8	101	100	11·2	11·1	99	100												
87	F	NP	...	0	5·0	5·8	113	109	9·1	8·8	95	98												
88	M	NP	B	..	5·11	5·6	93	95	8·4	7·8	92	96												
89	M	NP	B	..	10·4	6·8	64	80	11·6	7·6	65	82												
90	F	NP	...	..	8·0	7·4	92	95	14·9	9·3	63	84	15·6	11·1	74	90								
91	M	NP	B	..	9·0	6·9	75	86	9·6	8·4	88	94	9·11	6·7	66	81	11·11	8·8	72	87	13·6	8·4	61	82
92	M	NP	NB	2	8·1	5·9	71	82	8·8	6·10	78	88												
93	F	P	NB	6	15·0	9·6	63	85	17·8	10·0	67	83												
94	M	P	B	5	12·0	9·0	75	89	12·6	9	72	87												
95	M	P	B	11	15·6	12·10	85	95	16·0	11·11	79	92	17·9	12·9	85	91								
96	M	NP	B	8	9·10	5·8	58	74	11·9	7·2	61	79	12·6	7·2	57	78								
97	F	P	NB	..	12·9	6·2	48	71	12·11	6·8	51	74												
98	F	NP	NB	5	5·3	6·0	114	109	7·3	7·2	99	99	10·8	10·0	94	97	15·6	14·7	98	98	18·10	16·3	108	97
99	M	NP	B	2	10·8	5·6	51	70	11·1	5·8	51	71												
100	M	NP	B	..	7·4	7·4	100	100	8·1	8·6	105	103	8·9	9·1	104	102	10·3	8·10	86	94	15·7	11·4	75	90
101	M	NP	B	..	11·5	7·0	61	79	13·0	7·8	59	80												
102	M	NP	...	..	8·11	9·4	105	102	9·6	9·6	100	100												
103	F	NP	...	13	14·5	11·4	78	92	14·10	12·1	81	94	15·3	12·5	82	94								
104	F	NP	NB	..	7·6	6·2	81	89	9·2	6·10	75	86	10·0	7·4	73	86	14·5	11·4	79	92				
105	M	NP	...	..	10·3	7·2	70	84	11·2	8·1	72	86	13·9	9·5	68	87	15·9	11·1	74	89	20·4	10·10	72	84
106	F	NP	...	13	14·10	13·10	93	98	15·7	14·9	98	99												
107	M	P	B	2	7·11	5·10	74	84	15·4	9·0	60	82												
108	M	P	NB	..	23·5	17·8	117	96	24·6	16·5	109	94												

[illegible] indicates participation, NP no participation [illegible]

facts as well as common observation but has said that "the curve is a theoretical one" and that "there is no definite proof, because we lack equal units for the measurement of intelligence." Freeman [21] has pointed out that the shape of the curve depends on the nature of the ability tested or on the difficulty or range of difficulty of the tests used. Heinis,[18a] in developing his personal constant, presupposed a logarithmic curve of mental growth. Kuhlmann [18c] also assumed a curve of negative acceleration.

On the other hand, Thurstone and Ackerson,[22] after equating the units, concluded from their study that the curve of growth for the Stanford-Binet test is an ogive, being positively accelerated up to about 10 years and then negatively accelerated and becoming asymptotic at about 15 years.

It is clear that before it is possible to make any valid comparison between the mental growth of children who have had encephalitis and the mental growth of normal children it is necessary to know the shape of the curve of mental growth for the normal child.

A brief glance at the raw data (table 1) will indicate that the children of this group were considerably retarded at the time of the first examination. (The average intelligence quotient for the entire group was 77.) This fact again introduces several difficulties. Were these children retarded before the attack, or did the disease produce the retardation? What is the nature of the mental growth of the retarded child? Does it yield the same general shape of curve as does that of the normal child? None of these questions has been answered satisfactorily.

Two methods of comparison have been used in this study: first, that of comparing the change and rate of change in intelligence quotient (I. Q.); second, that of comparing the change and rate of change in personal constant (P. C.). Neither of these methods is completely satisfactory. The first is based on the assumption that the growth of intelligence (M. A.) with chronological age (C. A.) is represented as a straight line at an angle of 45 degrees with the abscissa for the average child. The second is based on the theoretical curve of growth derived by Heinis.

AMOUNT AND RATE OF CHANGE FOR THE TOTAL GROUP

The entire group included 108 persons, whose chronological ages at the time of the first examination ranged from 2 to 26 years, with a mean of 12.2 years. Table 2 presents the average intelligence quotients derived from the successive tests for the entire group. These averages

21. Freeman, F. N.: Mental Tests, Boston, Houghton Mifflin Company, 1926, p. 329.

22. Thurstone, L. L., and Ackerson, L.: The Mental Growth Curve for the Binet Tests, J. Educ. Psychol. **20**:569 (Nov.) 1929.

indicate that most of the children were to be classified as "dull" or "borderline defective" at the time of the first examination. This low initial rating subsequent to the onset may have been a result of the disease. This cannot be determined, since there was no rating prior to the onset.[23] However, most of the cases were selected from the files of the Institute for Juvenile Research, and the average rating for 5,000 consecutive children examined at the Institute was 79 (Ackerson [24]), just slightly above the average for this group. The low average rating for this group may be due to factors determining the selective reference to the Institute of retarded children, whether they are afflicted with encephalitis or not. Without exception, however, there is a decrease in the average intelligence quotient from one examination to another.

Table 3 gives the mean (algebraic) difference in intelligence quotient and in personal constant between each successive pair of tests. In each instance there is a decrease.

TABLE 2.—*Average Intelligence Quotient Derived from the Successive Tests for Groups with Various Numbers of Tests*

Group Given	Number of Subjects	Test					Difference
		1st	2d	3d	4th	5th	
		Average Intelligence Quotient					
Two tests or more	108	77	73	..	..	..	— 4
Three tests or more	49	83	78	77	..	..	— 6
Four tests or more	28	80	75	73	72	..	— 8
Five tests or more	21	82	78	76	73	68	—14

The length of time between the first and the last test ranged from a few months to thirteen years and eight months. If the disease had a progressive effect on change in intelligence, the amount of change in rating would be a function of the amount of time between the tests. A drop of 20 points in one year means something different from a drop of 20 points in twenty years. We were able from the data to compute a yearly rate of change. This was done by dividing the difference in rating between successive tests by the amount of time between the tests. A child who had had five tests would have four different rates; between the first and the second test there might be a gain and a positive

23. There was one case in which a rating prior to the onset was available. The intelligence quotient prior to the onset was 88 and the only rating subsequent to the onset 51. There were three cases in which ratings for siblings were available. In one case the initial rating subsequent to the onset was 76 and the rating for a sibling 108; in another case the intelligence quotient was 51 and that for a sibling 87, and in a third case the intelligence quotient was 76 and that for a sibling 59.

24. Ackerson, L.: Children's Behavior Problems, Chicago, University of Chicago Press, 1931.

rate and between the second and third tests a loss and a negative rate. There were 206 rates for the total group. The average rate of change per year in terms of intelligence quotient was a decrease of 2.34 ± 0.46;[25] and in terms of personal constant, a decrease of 1.40 ± 0.28 (table 7). The average length of time between the first and last test for the entire group was three and one-half years. It may be maintained that part of this large yearly decrease in intelligence quotient was due to the inevitable tendency for the intelligence quotient of "dull" children to show decrease because the mental growth does not conform to a straight line curve, which is assumed by the formula for the intelligence quotient (M. A./C. A.). The same tendency, however, is found for the personal constant, which assumes a growth curve of negative acceleration.

TABLE 3.—*Mean (Algebraic) Difference in Intelligence Quotient and in Personal Constant Between the Successive Tests for the Total Group* *

Tests Compared	Number of Subjects	Mean Difference in Intelligence Quotient	Mean Difference in Personal Constant
1st and 2d	108	−3.6 ± 0.66	−1.5 ± 0.32
2d and 3d	49	−1.7 ± 0.79	−1.0 ± 0.41
3d and 4th	28	−3.0 ± 0.96	−1.6 ± 0.57
4th and 5th	21	−4.5 ± 1.34	−3.5 ± 0.82

* Last rating minus first rating.

COMPARISON OF SUBJECTS WITH AND THOSE WITHOUT PARKINSONISM

There is considerable disagreement among investigators regarding the relative effect of the disease on general intelligence in cases in which signs of parkinsonism appear and in those in which they do not. It is the purpose in this section to consider this question.

Table 4 gives the number of subjects, the mean chronological age, the mean intelligence quotient and the standard deviation of the distribution of intelligence quotients on each of the successive tests for subjects with and subjects without signs of parkinsonism. Those with parkinsonism were an average of 4 years older at the time of the first examination than were those without parkinsonism. (This is of some

25. There may be some doubt about the applicability of the usual formula for the probable error of a mean ($0.6745\ \sigma_{diff.}\ \sqrt{N}$) in this situation, since we are not dealing exclusively with independent observations. Since we have grouped together differences between successive tests of the same subject (first and second, second and third, etc.), any error in any test except the first or the last will affect two differences. It would appear, however, since such an error would usually increase any disparity between the differences, that as a result of this method we err on the side of safety by making the P.E.$_m$ unduly large.

significance in interpreting the data of table 5.) It may also be noted that for those with parkinsonism the rating on the initial test was 10 points lower than for those without parkinsonism.

So far as could be determined from the records, the average chronological age at the time of the onset for those with parkinsonism was 8.5 years and for those without parkinsonism 6.7 years. Those with parkinsonism were an average of 1.8 ± 0.64 years older at the time of the onset.

Table 5 gives the mean (algebraic) difference in intelligence quotient and in personal constant between successive tests for those with

TABLE 4.—*Data on the Successive Tests for the Group With and the Group Without Parkinsonism* *

	Group With Parkinsonism				Group Without Parkinsonism			
Test	No. of Subjects	Mean C.A.	Mean I.Q.	S.D.I.Q.	No. of Subjects	Mean C.A.	Mean I.Q.	S.D.I.Q.
1st	40	14.7	71	15.4	68	10.7	81	18.3
2d	40	16.7	68	15.4	68	12.4	75	18.9
3d	15	16.3	76	18.8	34	12.6	76	16.0
4th	7	16.4	67	17.2	21	13.8	71	15.7
5th	6	17.7	66	13.5	15	16.5	69	16.4

* Only the first and second tests involve the same children.

TABLE 5.—*Mean (Algebraic) Difference in Intelligence Quotient and in Personal Constant Between the Successive Tests for the Group With and the Group Without Parkinsonism* *

	Group With Parkinsonism			Group Without Parkinsonism		
		Mean Difference in			Mean Difference in	
Pair of Tests	Number of Subjects	Intelligence Quotient	Personal Constant	Number of Subjects	Intelligence Quotient	Personal Constant
1st and 2d	40	−2.9	−1.7	68	−4.0	−1.6
2d and 3d	15	−0.7	−1.3	34	−2.1	−0.6
3d and 4th	7	−4.1	−2.9	21	−2.7	−1.0
4th and 5th	6	−3.0	−1.5	15	−5.1	−4.3
1st and last	40	−4.4	−3.0	68	−7.0	−3.2

* Last rating minus first rating.

and those without parkinsonism. Downward trends are indicated for both groups.

The average rate of change per year in intelligence quotient for the various levels of chronological age was determined for each group. No significant relation between chronological age and rate of change was found.

The average rate of change per year in intelligence quotient for each year after the onset was also determined for each of the groups. No relation was found either within or between the groups. So far as could be determined from the data, the rate of change at ten years after

the onset was neither greater nor less than that at two years after the onset for either group. The average rate of change was slightly greater for those without parkinsonism than for those with parkinsonism.

A distribution of the amount of change in intelligence quotient between the first and the last test is given in table 6. The time between the tests is disregarded. It ranged from a few months to thirteen years. The distribution is decidedly skewed in the negative direction. Of the 108 subjects, 48, or 44.4 per cent, showed a decrease in intelligence quotient of more than 4 points; 43, or 39.8 per cent, showed no change greater than would be expected by chance, and 17, or 15.7 per cent, showed an increase of more than 4 points. It is instructive to note, however, that a number did show improvement. It is interesting to speculate regarding the possibility that these increases were due to improvement after the acute attack.

TABLE 6.—*Distribution of the Amount of Change in Intelligence Quotient Between the First and the Last Test for the Group With and the Group Without Parkinsonism and for the Total Group*

Amount of Change	Group With Parkinsonism	Group Without Parkinsonism	Total Group	
20 to 23	1	0	1	
16 to 19	0	2	2	
12 to 15	2	2	4	15.7%
8 to 11	3	0	3	
4 to 7	3	4	7	
0 to 3	7	11	18	39.8%
−1 to −4	11	14	25	
−5 to −8	1	7	8	
−9 to −12	2	10	12	
−13 to −16	4	3	7	
−17 to −20	2	7	9	44.4%
−21 to −24	0	6	6	
−25 to −28	4	1	5	
−29 to −32	0	1	1	

In a study of 700 "morons," who might be comparable with members of this group as far as their general level of intelligence is concerned, Chipman [26] found that 24 per cent showed a decrease in intelligence quotient of more than 4 points; that 66 per cent showed no change greater than would be expected by chance, and that 10 per cent showed an increase of more than 4 points. Chipman has not indicated the length of time between the examinations. The more pronounced decreases in intelligence quotient for the encephalitic children suggest that the loss is not due solely to the inevitable tendency for the intelligence quotient of "dull" children to decrease.

Table 7 gives the average (algebraic) rate of change per year in intelligence quotient and in personal constant for the group with and

26. Chipman, C. E.: The Constancy of the Intelligence Quotient of Mental Defectives, Psychol. Clin. **18**:103 (May) 1929.

the group without parkinsonism as well as for the entire group. There is a yearly decrease in both intelligence quotient and personal constant of about the same amount for the group with and the group without parkinsonism. The yearly decrease in intelligence quotient is greater than the decrease in personal constant, but both show downward trends. The differences are statistically significant only for the entire group—that is, for the large number of subjects. There is no evidence of any greater decrease in intelligence for those with parkinsonism than for those without parkinsonism.

TABLE 7.—*Mean Rate of Change per Year in Intelligence Quotient and in Personal Constant Between the Successive Tests for the Group With and the Group Without Parkinsonism and for the Total Group*

Group	Number of Rates	Mean Rate of Change per Year in	
		Intelligence Quotient	Personal Constant
With parkinsonism	68	−2.38 ± 0.66	−1.54 ± 0.43
Without parkinsonism	138	−2.29 ± 0.61	−1.37 ± 0.36
Total	206	−2.34 ± 0.46	−1.40 ± 0.28

TABLE 8.—*Data on the Successive Tests for the Group With and the Group Without Behavior Disorder*

Test	Group With Behavior Disorder				Group Without Behavior Disorder			
	No. of Subjects	Mean C.A.	Mean I.Q.	S.D.I.Q.	No. of Subjects	Mean C.A.	Mean I.Q.	S.D.I.Q.
1st	41	12.0	76	15.9	37	12.2	79	17.6
2d	41	13.5	72	15.6	37	14.3	74	18.1
3d	20	14.0	73	13.6	13	13.2	82	19.0
4th	13	14.4	67	11.0	8	13.7	78	12.1
5th	8	16.5	60	10.9	7	16.1	79	16.4

COMPARISON OF SUBJECTS WITH AND THOSE WITHOUT BEHAVIOR DISORDER

As previously stated, the subjects who were classified as presenting evidence of behavior disorder were those who had gross disturbances of behavior, those whose disturbances seemed particularly characteristic of lethargic encephalitis and those in whose cases other explanations for the disturbances were not apparent in the history. Because of insufficient data, there were a number of children who could not be classified either in the group with or in the group without behavior disorder. The cases of these children were excluded from this part of the study.

The average age at the time of the onset was about the same for the two groups; for the group with behavior disorder it was 6.9 years, and for the group without, 7.2 years.

Some of the essential data regarding these two groups are given in table 8. The results of the first two tests only can be compared, since the results of the last three tests do not represent all the subjects included in these two groups. The chronological age at the time of the initial examination is about the same for the two groups; for the group with behavior disorder it is 12 years, and for the group without, 12.2 years. The average length of time between the first and the second test is one and one-half years for the group with behavior disorder, and two and one-tenth years for the group without behavior disorder. The average drop in intelligence quotient between the two tests is 4 points for the former group and 5 points for the latter. Thus, the drop in intelligence quotient in relation to time is slightly greater for the group with behavior disorder.

The average (algebraic) rate of change per year in intelligence quotient and in personal constant for each of these groups is given in table 9. The average yearly decrease is greater for the group with

TABLE 9.—*Mean (Algebraic) Rate of Change per Year in Intelligence Quotient and in Personal Constant Between the Successive Tests for the Group With and the Group Without Behavior Disorder*

Group	Number of Rates	Mean Rate of Change per Year in	
		Intelligence Quotient	Personal Constant
With behavior disorder	82	-3.55 ± 0.85	-1.85 ± 0.50
Without behavior disorder	65	-1.37 ± 0.63	-0.95 ± 0.38
Difference	..	-2.18 ± 1.09	-0.90 ± 0.62

behavior disorder than for the group without behavior disorder. The difference, however, while suggestive, is not statistically significant.

The relation of the incidence of behavior disorder to that of parkinsonism was investigated. So far as could be determined from the data, there was no evidence that behavior disorder occurred more frequently in the cases in which there appeared signs of parkinsonism than in those in which there did not. The tetrachoric correlation coefficient was -0.16 ± 0.11.

RELATION BETWEEN AGE AT ONSET AND CHANGE IN INTELLIGENCE

In this part of the investigation the subjects were divided into three groups: those in whom the onset of the disease occurred before the fifth birthday, those in whom it occurred between the fifth and the tenth birthday and those in whom it occurred after the tenth birthday. The number of children was too small to warrant a division into a larger number of groups. In some instances it was impossible to determine from the records the age at the time of the onset. When this was so,

the cases were excluded from this section of the study. Some of the data regarding the three groups are given in table 10. The data regarding the rate of change are presented in table 11.

Table 10 indicates that for the group in whom the onset occurred at an age below 5 years the rating on the initial test is lower than for either of the other groups. This may be due to the fact that for this group the length of time between the onset and the first test was greater than for either of the other groups.

Table 11 presents the mean (algebraic) rate of change in both intelligence quotient and personal constant for each of these three groups and for the first and second groups combined. The rate of decrease in

TABLE 10.—*Data on Two Successive Tests for Groups of Various Ages at Time of Onset*

Group	1st Test				2d Test			
	No. of Subjects	Mean C.A.	Mean I.Q.	S.D.I.Q.	No. of Subjects	Mean C.A.	Mean I.Q.	S.D.I.Q.
Age at onset:								
0 to 4 yr.	21	9.3	75	17.7	21	10.7	72	17.0
5 to 9 yr.	39	11.7	78	18.2	39	13.7	71	16.7
10 yr. and over	24	16.2	76	14.6	24	17.7	78	17.7

TABLE 11.—*Mean (Algebraic) Rate of Change per Year in Intelligence Quotient and in Personal Constant Between the Successive Tests for Groups of Various Ages at Time of Onset*

Group	Number of Rates	Mean Rate of Change per Year in	
		Intelligence Quotient	Personal Constant
Age at onset:			
0 to 4 years	46	−3.5 ± 0.74	−1.11 ± 0.40
5 to 9 years	65	−3.77 ± 0.83	−2.54 ± 0.51
0 to 9 years	111	−3.62 ± 0.56	−2.01 ± 0.35
10 years and over	43	−0.81 ± 0.97	−1.28 ± 0.53
Difference	..	−2.81 ± 1.12	−0.73 ± 0.64

both intelligence quotient and personal constant is greater for the group with onset at an age of from 5 to 9 years than for the group with onset at an age of less than 5 years. The decrease in intelligence quotient is greater for each of these groups than for the group with onset at an age of 10 years or above. In terms of personal constant, however, the decrease is slightly greater for the group with onset at an age of 10 years or above than for the group with onset at an age of less than 5 years. There is, however, a greater decrease for the first and second groups combined than for the group with onset at an age of 10 years or above. While this comparison forms an interesting and suggestive contrast, the difference appears to be of doubtful significance statistically, at least in regard to the personal constant.

In general, there seems to be slight evidence that decrease in intelligence is more characteristic of the children in this group who acquired the disease before the age of 10 years than of those who were afflicted at a later age.

PROGRESSIVE IMPAIRMENT

In chart 1 is plotted the curve of mental age (M. A.) with chronological age (C. A.) for each of the children to whom three or more tests were given after the third and before the fifteenth birthday at intervals of a minimum of one and one-half years. The three tests

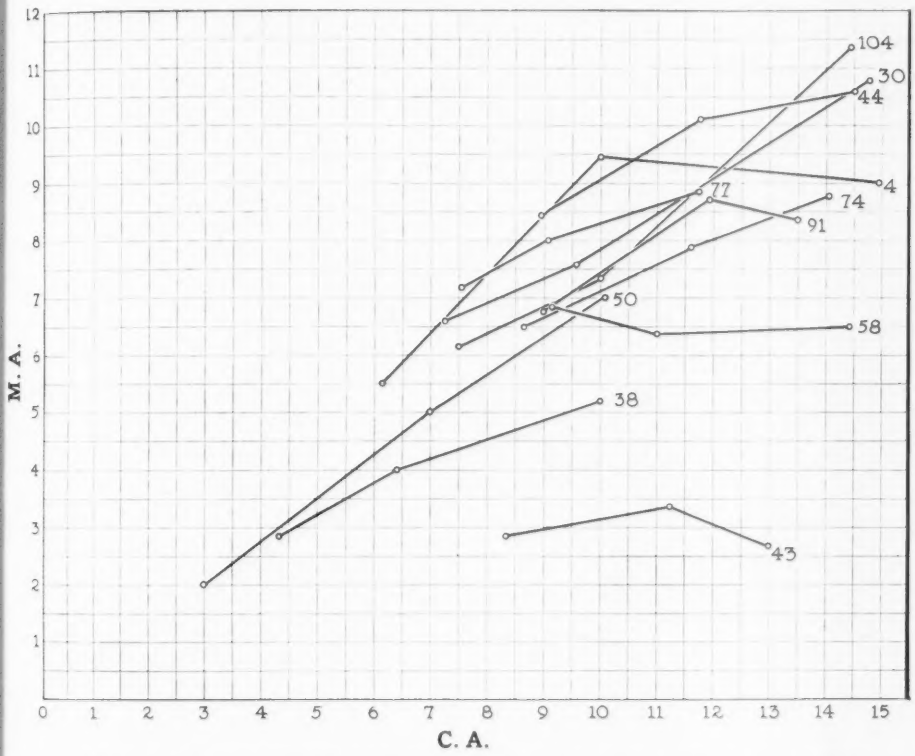

Chart 1.—Mental growth in terms of mental age units (Binet) for children to whom three or more tests were given after the third and before the fifteenth birthday at intervals of a minimum of one and one-half years.

represented are the first, the last and the one given nearest the middle of the interval between the first and the last.

The mere fact of a decrease in intelligence quotient or in personal constant would not establish the occurrence of progressive damage to the intelligence, since the acute phase of the disease might conceivably interfere less with the intelligence already developed than with the rate of further mental growth. If this were true, as the years passed there

would be an increasingly greater lag of mental age compared with chronological age and, consequently, a decrease in the intelligence quotient or in the personal constant. In such event, the curve of mental growth would be a straight line but would not pass through the origin. If, however, the damage to the intelligence is considered as continuing or as progressive in the chronic phase of the disease, and if it is assumed that the intelligence quotient is normally constant, the curve of mental growth would be a line angulated by a downward break of the

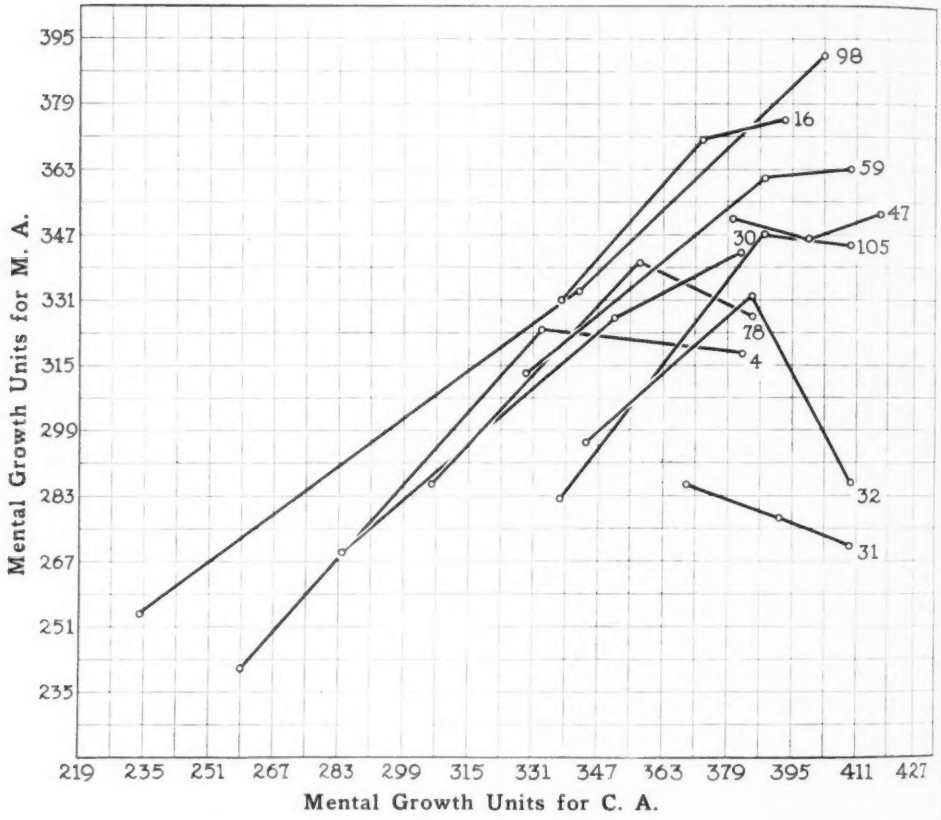

Chart 2.—Mental growth in terms of mental growth units (Heinis) for children to whom three or more tests were given after the third birthday at intervals of a minimum of three years.

terminal portion. This is the prevailing tendency in chart 1, and in it can be observed an indication that the damage to the intelligence in lethargic encephalitis is frequently progressive in the chronic state.

If it is assumed that the curve of mental growth is represented by Heinis' equation, as is implied by acceptance of the personal constant, rather than by the straight line implied in the assumption of a constant

intelligence quotient, there should be plotted the mental growth units for mental age against the mental growth units for chronological age. This is done in chart 2 for each of the children to whom three or more tests were given after the third birthday at intervals of a minimum of three years. The three tests represented are the first, the last and the one given nearest the middle of the interval between the first and the last. There was no reason for excluding tests given after the fifteenth birthday. Again the prevailing tendency is for lines to be angulated by downward displacement of the terminal portion. This may be interpreted not simply as due to a constant retardation of the process of growth but as representing the cumulative effect of slow, characteristically progressive damage to the brain.

CONCLUSIONS

There is indication of a slight, progressive decrease in intelligence, as determined by objective tests, for children afflicted with lethargic encephalitis.

There is no evidence of any greater decrease in intelligence for those with parkinsonism than for those without parkinsonism.

There is indication of a slightly greater decrease in intelligence for those in whom behavior disorder develops than for those in whom it does not. The difference, however, is not statistically reliable.

There is indication of a slightly greater decrease in intelligence for those who experience the onset of the disease before the age of 10 years than for those who experience the onset at a more mature age. The difference, however, is not statistically reliable.

Continued observation of a small number of subjects suggests that the decrease in intelligence, as determined by objective tests, is not to be explained solely as an effect of the acute attack of the disease but represents the effect of progressive damage to the brain.

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STUDIES OF FETAL RESPIRATORY MOVEMENTS

II. RECORDING METHODS

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Recently Rosenfeld and Snyder [1] transected the spinal cords of experimental animals in order to avoid the depressing action of anesthetics or analgesics when observing the intra-uterine respiration-like movements of fetuses. Observation of such fetal activity is not new; in fact, in the early part of this century a lively controversy occurred over the existence of fetal respiratory movements. It is not our purpose to discuss this particular phase of the subject at the present time, for we have done so in a previous communication.[2] It suffices to state that we are inclined to agree with Ahlfeld,[3] Reifferscheid [4] and Rosenfeld and Snyder [5] that such movements occur and that in all probability they are physiologic. Indeed, it is hard to reconcile oneself to the belief that the fetal respiratory tract in utero remains inert, awaiting only the proper stimulus to initiate its hitherto unpracticed mechanism at birth, while the cardiovascular system, with which it is so intimately associated, the gastro-intestinal tract and the kidneys function in intra-uterine life. However, regardless of what may be said of this, one way or another, we do know that in the animal in which the cord has been sectioned and the abdomen opened periodic and nearly rhythmic fetal movements, which simulate closely the normal respiratory movements of the neonatal animal, may be observed through the uterine wall. Furthermore, when the uterus has been incised and the fetuses viewed through the intact,

† Dr. Bonar died Dec. 18, 1937.

From the University of Utah School of Medicine.

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1. Rosenfeld, M., and Snyder, F. F.: Fetal Respiration in Rabbits, Proc. Soc. Exper. Biol. & Med. **33**:576, 1936.

2. Bonar, Barnet E.; Blumenfeld, Charles M., and Fenning, C.: Studies of Fetal Respiratory Movements: I. Historical and Modern Observations, Am. J. Dis. Child. **53**:1 (Jan.) 1938.

3. Ahlfeld, F.: Die intrauterine Tätigkeit der Thorax- und Zwerchfellmuskulatur, intrauterine Atmung, Monatschr. f. Geburtsh. u. Gynäk. **21**:143, 1905.

4. Reifferscheid, K.: Ueber intrauterine Atembewegungen des Foetus, Deutsche med. Wchnschr. **37**:877, 1911.

5. Snyder, F. F., and Rosenfeld, M.: Breathing of Amniotic Fluid as a Normal Function of Fetal Respiration, Proc. Soc. Exper. Biol. & Med. **36**:45, 1937.

transparent amniotic sacs, their respiratory actions, especially if marked, include opening and closing of the mouth and movement of the nares. Fetuses in which this movement has occurred for many minutes can be freed from the sac and will continue to live normally.

KYMOGRAPHIC METHODS

Several methods have been used to study such fetal movements. Earlier investigators observed them with the naked eye after exposing the uterus. Others tried to record the movements graphically through the unopened abdomen and uterus of the pregnant woman. Weber [6] and Ahlfeld were the first to use the kymograph for this purpose. They made tracings in which the fetal respiratory movements, the mother's respirations and pulse and the time were recorded, but not simultaneously. Reifferscheid repeated this work, with the kymograph recording time, maternal respiration, carotid pulse and fetal respiratory movements simultaneously. His curves showed positively that maternal aortic pulsation was not responsible for the movements. The use of ordinary kymographic methods is of value in the study of fetal respiratory activity, but there are several difficulties, chief among which are the mechanical ones encountered when so many recording tambours are used and the impossibility of making continuous records over long periods.

CINEMATOGRAPHIC METHODS

Rosenfeld and Snyder made motion pictures of fetal respiratory movements after opening the abdomen and exposing the uterus of a cord animal, and they were able to demonstrate clearly respiratory movements which they considered similar to the normal extra-uterine respiratory act. We have duplicated this work with colored motion pictures and have confirmed their observations to a large extent. However, it was found that while motion pictures could be used satisfactorily for demonstrating fetal respiratory activity, certain disadvantages existed. In the first place, timing was difficult, and by virtue of this the regularity or rhythm of the movements could not be determined accurately; in the second place, study of variations in the amplitude and the character of the movements was extremely difficult or nearly impossible; in the third place, accurate correlation of these movements with the maternal pulse and respiration, as well as with uterine contractions, could not be made. Therefore, a graphic method which would remove these difficulties seemed desirable, particularly if the effects of anesthetics and analgesics

6. Weber, cited by Ahlfeld.[3]

on the fetal respiratory mechanism were to be studied. An instrument that may be adapted to this purpose has been devised and described by Fenning.[7]

OSCILLATOCAPACIGRAPHIC METHOD

Briefly and diagrammatically (fig. 1) the oscillatocapacigraph consists of a vacuum tube circuit, B_1, connected with a metal plate (a modified Hartley oscillator circuit). The oscillator, B_1, is in turn connected with a galvanometer, the mirror of which is held in the neutral position by opposing electrical currents of equal strength (a zero shunt galvanometer) derived from the oscillator, B_1, and an external source, B_2. These currents are adjusted to neutralize one another—that is, B_1 equals B_2, when the subject and the plate are placed in position 1. The mirror of

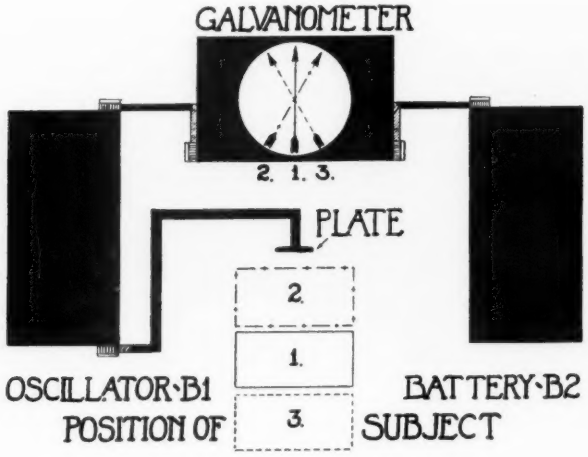

Fig. 1.—Schematic diagram of the oscillatocapacigraph.

the galvanometer, represented by the arrow in the diagram, then stands at position 1. When the subject approaches the plate to occupy position 2, B_1 overbalances B_2, and the mirror of the galvanometer assumes position 2. When the subject recedes from the plate to position 3, B_2 overbalances B_1, and the mirror of the galvanometer assumes position 3. By means of a suitable system of illumination, the deflections of the mirror of the galvanometer are projected on photosensitive paper and recorded. The recorder we are using at present permits us to run 100 feet (30 meters) of paper before refilling is necessary. This makes it possible to record movements for several hours.

7. Fenning, C.: A New Method of Recording Physiologic Activities: I. Recording Respiration in Small Animals, J. Lab. & Clin. Med. **22**:1279, 1937. Fenning, C., and Bonar, B. E.: A New Method of Recording Physiologic Activities: II. Simultaneous Recording of Maternal Respiration, Intrauterine Fetal Respiration and Uterine Contractions, ibid. **22**:1280, 1937.

DESCRIPTION OF RECORDS

Using the instrument described, we have been able to record the following more or less simultaneous activities of the mother and the fetus: (1) maternal respirations; (2) uterine contractions; (3) fetal movements, and (4) fetal respiratory activity.

The spinal cord of an experimental animal is transected at the mid-thoracic level, in order to anesthetize the abdominal wall without causing the depressing effects of ordinary anesthetics or analgesics. The abdomen is then opened and the uterus delivered through the incision into physiologic solution of sodium chloride at a temperature of from 37 to 38 C. The small metal plate connected with the instrument is placed a centimeter or less from the uterus, depending on the size of the deflection

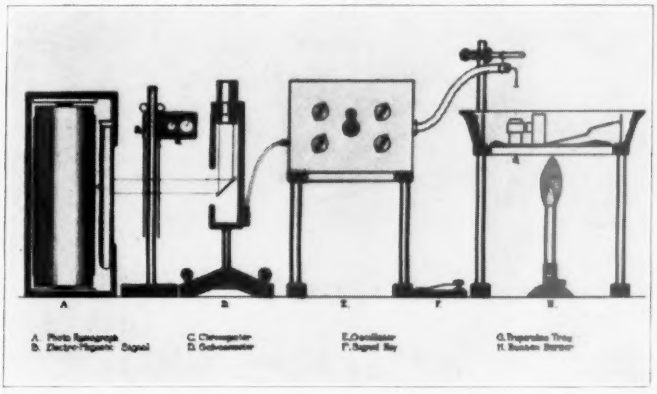

Fig. 2.—Complete apparatus.

desired on the record. Time is recorded with a Jacquet chronometer, and a telegraph signal marker is used to indicate the different movements of the fetus. The complete apparatus is shown in figure 2.

Figure 3 is a record of maternal respirations, produced indirectly by the insignificant movements of the uterus transmitted from the rise and fall of the abdominal contents during breathing. When the uterus is pushed toward the plate there is an upward deflection, and when it recedes the deflection is downward.

Figure 4 is a record of maternal respirations and uterine contractions. It should be noted that as the uterine wave reaches its summit—that is, when the contracting uterus squeezes the enclosed fetus nearer to the plate—the deflection is upward, and when the uterus relaxes it is downward. Owing to the fact that during a uterine contraction the uterus is nearer to the plate, the maternal respiratory waves have greater amplitude at this time than when the uterus recedes.

Figure 5 is a tracing of maternal respirations, uterine contractions and a strong fetal movement. Each of these movements makes a curve so characteristic that it is identified with ease. Particularly is this true of the impulsive jerks of the fetal body or limbs, which produce one or more diphasic curves of great amplitude.

Figure 6 is a record of maternal respirations, uterine contractions, several nearly rhythmic fetal respiratory movements and an occasional fetal movement. On closer analysis we have distinguished three differ-

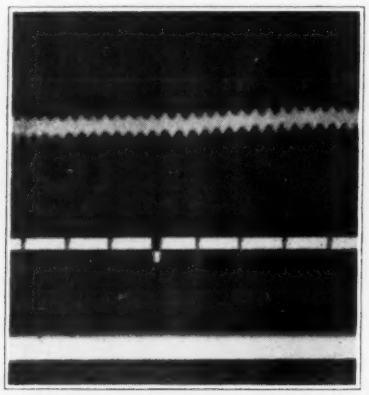

Fig. 3.—Record of maternal respirations in a rat.

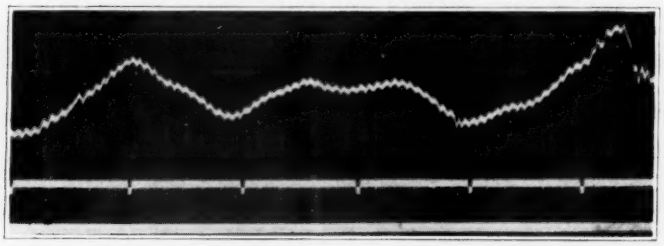

Fig. 4.—Record of maternal respirations and of the slow, undulating uterine contractions in a rat.

ent curves produced by the fetal respiratory act in the rat. These are shown in figure 7. The first (*a*) is a monophasic curve with the deflection downward; the second (*b*), a monophasic curve with the deflection upward, and the third (*c*), a diphasic curve with an initial deflection which may be either downward or upward. There are several possible explanations for the variations noted. If the plate is over the abdomen of the fetus, a diaphragmatic contraction will expand the abdomen, and the curve will be monophasic with the deflection directed upward. However, if the respiratory act is initiated by contraction of the thoracic

musculature, the deflection, while monophasic, will be directed downward—that is, the abdomen will retract. When the plate is placed over the thorax, a diaphragmatic contraction will cause the chest to recede, and a downward monophasic deflection will be recorded. If the respiratory act is initiated by the thoracic musculature, an upward monophasic deflection will occur. In the diphasic curves the initial deflection is dependent on the position of the plate and the character of the first respiratory impulse—that is, on whether the initial movement is diaphragmatic or thoracic. With the plate over the thorax and an initial

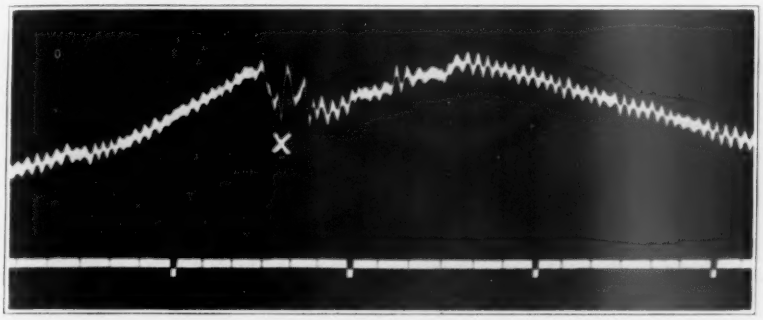

Fig. 5.—Record of maternal respirations, uterine contraction and a fetal movement in a rat (*X*). The last is represented by the great diphasic deflections.

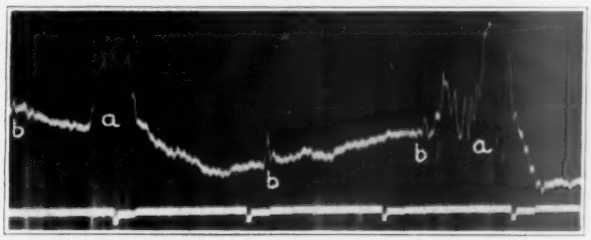

Fig. 6.—Record of maternal respirations, uterine contractions, occasional fetal movements (*a*) and several fetal respiratory movements (*b*) in a rat.

diaphragmatic contraction, there are a corresponding retraction of the chest and a downward deflection. If this is followed by activity of the thoracic musculature and enlargement of the chest, the latter half of the deflection is upward. Theoretically, if the plate was placed midway between the thorax and the abdomen, the resultant of the contraction should be zero, and there would be no record of the respiratory act, provided both diaphragmatic and thoracic movements occurred simultaneously. In such an instance the observer noted a respiratory movement which either was not recorded or else was obscured by the maternal respiratory curves. While these characteristics are of importance in

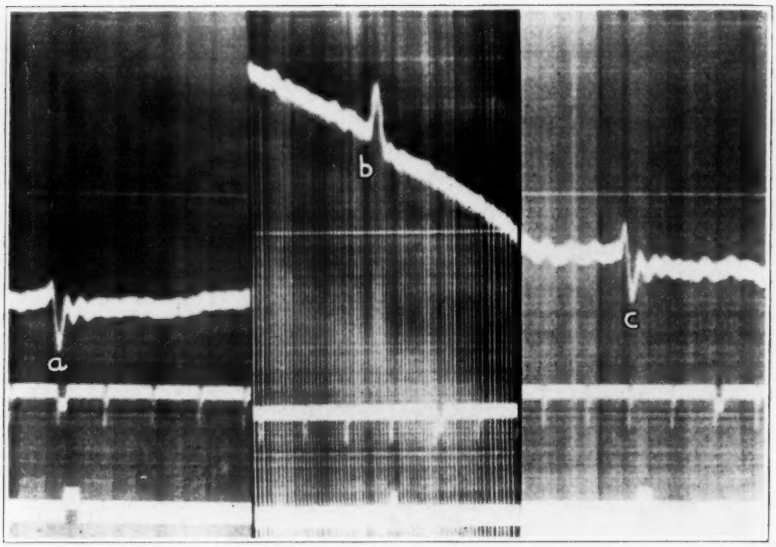

Fig. 7.—Three types of fetal respiratory deflections in a rat: (*a*) monophasic with deflection downward; (*b*) monophasic with deflection upward, and (*c*) diphasic (initial deflection upward).

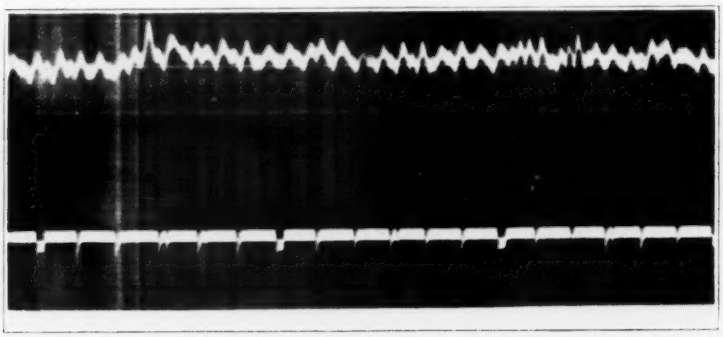

Fig. 8.—Record of maternal respirations of unopened abdomen of a guinea-pig.

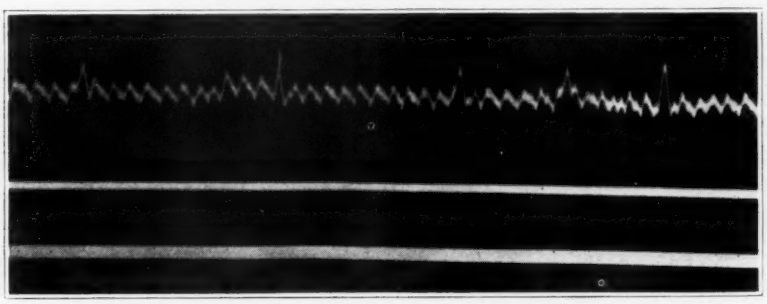

Fig. 9.—Record of maternal respirations of unopened abdomen of a guinea-pig, with superimposed deflections resembling fetal respiratory movements.

analyzing the nature of the respiratory act in the fetus, from the standpoint of determining the rate, they are not so valuable. We have also noted that after depression of the thorax from contraction of the diaphragm there is a return to the original neutral position. In other words, as air is absent in the passages, the chest does not expand as it does in the air-breathing animal. The character of the curves as described is of assistance in determining the position of the plate with respect to the abdomen or the chest. The variability in type of the curves in different records is probably due to the position of the plate.

Figure 8 is a record of maternal respirations in a guinea-pig the abdomen of which had not been opened. The plate was over the abdomen. Figure 9, made under the same conditions, is a record of maternal respirations and fetal impulses similar to those previously obtained from the exposed uteri of rats and of rabbits. This record furnishes further evidence of the existence normally of fetal respiratory movements in utero.

SUMMARY AND CONCLUSION

The various methods of observing and recording fetal respiratory movements in utero are discussed and criticized.

The oscillatocapacigraphic method, which makes it possible to record on one curve the maternal respiratory movements, the uterine contractions, the fetal movements and the fetal respiratory movements, is described, and a few records obtained are shown.

This method appears to be the best approach at the present time to the study of fetal respiratory activity. Studies made with this instrument should be of value in obtaining more accurate results in investigating many of the problems related to the activity of the fetus in utero.

University of Utah.

Case Reports

HYPOGLYCEMIA OF THE NEW-BORN

ASSOCIATED WITH HYPERTROPHY AND HYPERPLASIA OF THE ISLANDS OF LANGERHANS

HENRY RASCOFF, M.D.

JACOB S. BEILLY, M.D.

AND

MENDEL JACOBI, M.D.

BROOKLYN

There are few reports in the literature of hypoglycemia in the new-born due to hyperplasia and hypertrophy of the islands of Langerhans. In 1920 Dubreuil and Andérodias [1] first described these changes in the islands in a fetus of a diabetic mother. Subsequently similar reports have been made by Wiener,[2] Gray and Feemster,[3] Schretter and Nevinny,[4] Skipper [5] and Gordon.[6]

REPORT OF A CASE

G., a boy, was born on Oct. 19, 1936, at 1 p. m., with a difficult delivery. His weight at birth was 11 pounds and 2 ounces (5,046 Gm.). The mother had had two previous pregnancies; the first came to term with the birth of a living child, the second ended in a miscarriage after seven months' gestation. During the first trimester of the third pregnancy there was a loss of weight of 18 pounds (8 Kg.), and the patient felt tired and worn. Urinalysis did not reveal any abnormal findings. Chemical examination of the blood was not done. The patient was treated to prevent a recurrence of the miscarriage and was given iron medication parenterally to correct the asthenia. She improved, regaining the lost weight rapidly, and felt stronger during the succeeding months.

The delivery was delayed considerably because of interruption of the normal mechanism of labor when the shoulders failed to engage. On manipulation this condition was corrected and delivery completed. The baby was born asphyxiated.

From the Department of Pathology, Beth-El Hospital.

1. Dubreuil, G., and Andérodias, A.: Compt. rend. Soc. de biol. **83**:1490, 1920.

2. Wiener, H. J.: Am. J. Obst. & Gynec. **7**:710, 1924.

3. Gray, S. H., and Feemster, L. C.: Compensatory Hypertrophy and Hyperplasia of the Islands of Langerhans in Pancreas of Child Born of Diabetic Mother, Arch. Path. **1**:348 (March) 1926.

4. Schretter, G., and Nevinny, H.: Arch. f. Gynäk. **143**:465, 1930.

5. Skipper, E.: Quart. J. Med. **2**:353, 1933.

6. Gordon, W. H. J.: J. Michigan M. Soc. **34**:167, 1935.

Summary of Recorded Cases of Fetal Hyperplasia and Hypertrophy of the Pancreas

Case	Date of Report	Author	Condition of Mother	Clinical Course	Birth Weight, Gm.	Microscopic Appearance of Pancreas*	Changes in Other Organs
1	1920	Dubreuil and Anderodias..	Severe diabetes	Following induced labor, child lived only a few hours	5,050	Hypertrophy and hyperplasia, 20-30 times normal amount of islet tissue	Enlargement of liver
2	1924	Weiner.....	Severe diabetes	Premature stillborn	1,900	Islets surrounded by edematous network of connective tissue; some islets larger than normal	None
3	1926	Gray and Feemster.....	Severe diabetes	Born prematurely at 8th month; at birth respiration and cry spontaneous; on 3d day vomited portions of each feeding; on 4th day peculiar pasty color, temperature was 38.36 C. (100.9 F.); found dead that evening; blood sugar on 3d day 67 mg. per 100 cc.	3,300	Hypertrophy and hyperplasia, of islet cells, 24 times normal size	Hemorrhage and necrosis of adrenals
4	1930	Schretter and Nevinny.....	Severe diabetes	Spontaneous delivery; sugar content of blood taken from umbilical artery at birth 62 mg.; 5½ hours after birth sugar content of capillary blood 52 mg., 5th day 62 mg., 8th day 106 mg., 12th day 95 mg., 16th day 192 mg.; died on 32d day of congenital heart disease	4,750	Hypertrophy and hyperplasia of islet cells	
5	1933	Skipper.....	Severe diabetes	Cesarean section at term; died in few minutes	4,760	Hypertrophy of islands of Langerhans	
6	1933	Skipper.....	Severe diabetes	Cesarean section—premature; died in 3 hours	2,880	Hypertrophy of islands of Langerhans	
7	1935	Gordon.....	Severe diabetes	Stillbirth at 8 months	"Large"	In all three cases, hypertrophy and hyperplasia of the insular tissue, amount being 6-8 times normal; marked infiltration of eosinophils in and around the cells	
8	1935	Gordon.....	Uncontrolled diabetes	Cesarean section; died in 12 hours; sugar content of heart blood too low to read	2,500		
9	1935	Gordon.....	Uncontrolled diabetes	Cesarean section at 8½ months; died 14 hours after birth; sugar in blood from heart 40 mg. per 100 cc.	4,800		
10	1936	Rascoff, Beilly and Jacobi	Latent diabetes	Full term difficult delivery—required resuscitation; lived 13 hours	5,280	Hypertrophy and hyperplasia of islet cells with eosinophilic and leukocytic infiltration	Adrenal hemorrhage

* The macroscopic appearance of the pancreas was normal in all cases.

Resuscitation was attempted with the use of alternate hot and cold baths, two ampules of alpha-lobeline given intramuscularly and mouth to mouth inhalation, but the child did not cry or breathe regularly. When seen by one of us (H. R.) at 2:20 p. m., one hour and twenty minutes after birth, he presented the following picture: He was excessively fat and was breathing irregularly and with difficulty. No tremors or convulsions were present. There was good muscle tone in the extremities. The anterior fontanel was not bulging. There was persistent, deep cyanosis of the face. The remaining surface of the skin was slightly cyanotic. The heart sounds were not rapid and were of good quality. Clinical examination of the chest revealed severe atelectasis of both lungs. No abdominal masses were palpable; the liver was somewhat enlarged. The child was given a mixture of 95 per cent oxygen and 5 per cent carbon dioxide continuously through a Henderson mask closely applied to the face. After twenty minutes the respirations were regular and goodly portions of both lungs were aerated. At this time the cry was strong and not cranial in pitch, and the child had a strong sucking reflex. In view of the excellent response to resuscitative measures, a good prognosis was given. One hour later the infant went into collapse; the temperature was 104 F. This time it was necessary to insufflate the bronchi directly by means of the Flagg apparatus before resuscitation was successful. In addition, 2 minims (0.12 cc.) of epinephrine was given subcutaneously. Again the lungs became well aerated and the breathing fairly regular, with a sound cry and a good sucking reflex. All these signs were, however, not as strong as before. A test for capillary blood sugar done at this time showed 27 mg. per hundred cubic centimeters of blood. In view of the hypoglycemia and evident dehydration, 100 cc. of a 10 per cent solution of dextrose was given intravenously. The child did not seem to react to the infusion. There was a tendency to sink into a comatose condition, from which he could be awakened slightly by the use of inhalation therapy. The periods of unconsciousness grew more frequent and longer and the response to therapy steadily diminished; the heart sounds became weaker. The infant died thirteen hours after delivery.

Gross Postmortem Examination.—This was performed one hour after death. The body was that of a well developed, extremely cyanotic new-born boy, weighing 11 pounds (4,990 Gm.) and possessing an unusually abundant deposit of subcutaneous fat on the trunk and limbs. The body measured 22 inches (56 cm.) in length, 35 cm. in occipito-frontal circumference, 42 cm. in chest circumference, 21 cm. in circumference at the midthigh and 14 cm. in circumference at the midarm. The hair on the head was thick. The umbilicus was clean and the ears and nose devoid of discoloration or discharge. The body was warm; no rigor was present.

The lungs were largely atelectatic. No tracheobronchial obstruction was present. The heart weighed 51 Gm. Its left border was almost in the axillary line; the right border, a little to the right of the midline. The foramen ovale and ductus arteriosus were patent. The endocardium, myocardium, pericardium, valves and aorta with its branches showed no gross anatomic changes. The thymus was grossly normal.

The panniculus adiposus was 1 cm. thick. The liver weighed 220 Gm. Its right and left lobes were equal in size, the capsule was glistening, the entire organ was firm and its edges were rounded. On section, the lobulation appeared indistinct. The biliary system and the entire gastro-intestinal tract were grossly normal. The spleen was soft, weighed 15 Gm. and showed the follicles distinctly on section. The pancreas weighed 3 Gm. and was firm and normally lobulated; its ducts were patent. The kidneys were grossly normal, as were the ureters and

bladder. The right adrenal gland measured 4 by 3 by 2 cm.; its cortex was normal; there was some medullary autolysis. The left adrenal gland, measuring 4 by 3.5 by 2 cm., had been converted into a thin-walled sac filled with blood clot; a small piece of cortex was grossly recognizable in the wall of the sac at its upper pole. The scalp and skull were grossly normal and the dura and brain grossly intact; no hemorrhages were present.

Microscopic Examination.—Multiple sections of the pancreas all presented a similar picture. The fibrous tissue running between groups of acini, i. e., the interlobular stroma, was edematous. There was some increase in poorly cellular fibrous tissue about the vessels and ducts, but these structures were everywhere distinctly demarcated from the accompanying or surrounding fibrous tissue. The

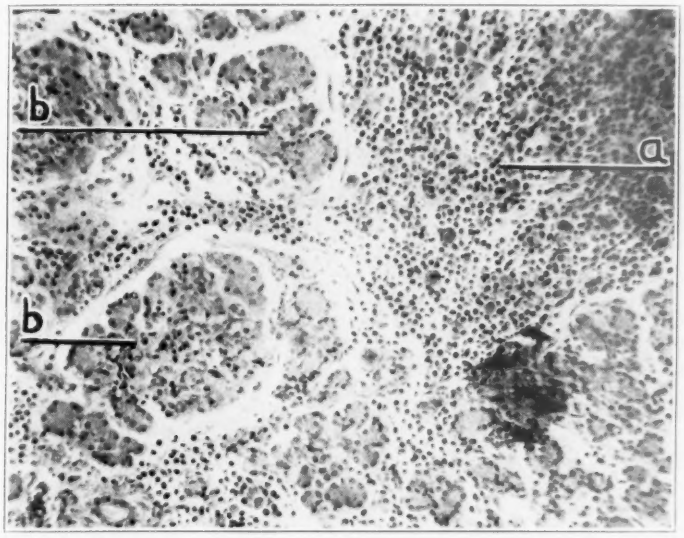

Fig. 1.—Topographic photomicrograph (× 10) of the pancreas, showing dense interstitial cellular infiltration (*a*) in which no pancreatic elements are present. The infiltrate extends between two large islands of Langerhans (*b*) and between pancreatic lobules.

acini were normal and the ducts showed no changes. The islands of Langerhans were remarkably numerous and large, all being from four to six times the usual fetal size, and instead of being compact and of medullary form they were lattice-like in appearance. The hyperplastic cells were chiefly of the beta type (Bensley's stain). The islands were made up of strands forming a mesh, single or double layers of polygonal cells merging with columnar cells in ductlike arrangement. In the stroma of loose fibrous tissue there was an extensive dense infiltration with polymorphonuclear leukocytes consisting chiefly of eosinophils and occasional large histiocytes (fig. 1). This infiltration in places extended between individual acini and into the islands. This cellular infiltrate in places was so dense and focal as to form a nodule of eosinophils, all mature, among which no acinar or islet tissue was visible. Even in or near such nodules there was no necrosis of tissue or atrophy of adjoining acini, so that even though the acini appeared to be somewhat separated by the eosinophil-containing interstitial tissue,

their lobules were perfectly regular; the acini were not atrophic, and their granules of zymogen were well stained and distinct. The eosinophilic infiltrate was also present within the islets of Langerhans and was particularly noticeable around these islets; the interstitial (interlobular) infiltrate seemed to spread from this region and to be directly continuous with it (fig. 2). Within the islets the eosinophils were frequently seen distending the capillaries; extracapillary eosinophils also were present within the islet cords (fig. 3). It is remarkable that, though evidence of active myelopoiesis was present in other organs, such as the liver, only in the pancreatic sections were eosinophils so noticeable. Here, in fact, they were virtually visible alone. The vessels showed no intrinsic changes.

Sections through the umbilical cord showed no evidence of inflammatory infiltration. Outside the vein there was considerable extravasated blood.

The lobular architecture of the liver was difficult to discern because of the extreme vacuolation of the cords (these vacuoles were composed of neutral fat; there were extremely few glycogen granules in the hepatic cells, as demonstrated by Best's stain) and the marked distention of the sinusoids and portal fields with immature red and white blood cells.

The lungs showed severe congestion, patchy atelectasis and alveolar distention, occasional alveoli containing a few histiocytes and erythrocytes and squamous epithelial débris.

The heart showed the myocardial fibers to be almost totally devoid of glycogen (Best's stain).

The spleen, thymus, thyroid, skin and brain showed no histologic changes.

The tubular cells of the kidney contained no granules of glycogen. The tubular lumens were moderately distended with red cell casts.

Several sections of the adrenal glands showed intact and well defined cortex and medulla. In other sections the medulla was replaced by recent hemorrhage, and the cortical zona fasciculata was congested; in still other areas the glomerular zone alone was not infiltrated with blood.

The Mother's Record.—In view of the insular changes in the new-born child, we examined closely the postpartum record of the mother, but found no symptoms of diabetes. Two months later a sugar tolerance test of the mother was done; the curve was like that of a moderately diabetic patient.

Response of Mother to Dextrose Tolerance Test (100 Gm. by Mouth)

	Blood Sugar	Urine Sugar
Fasting	130	None
½ hour	174	None
1½ hours	182	None
2½ hours	198	Trace
3½ hours	146	None

COMMENT

We have reviewed the other cases of hypertrophic changes in the islet in the literature to determine their similarities and differences.

Etiology and Pathology.—In all confirmed cases of hypertrophy or hyperplasia of the islands of Langerhans of the fetus or of the new-born infant, the mother has had severe or uncontrolled diabetes

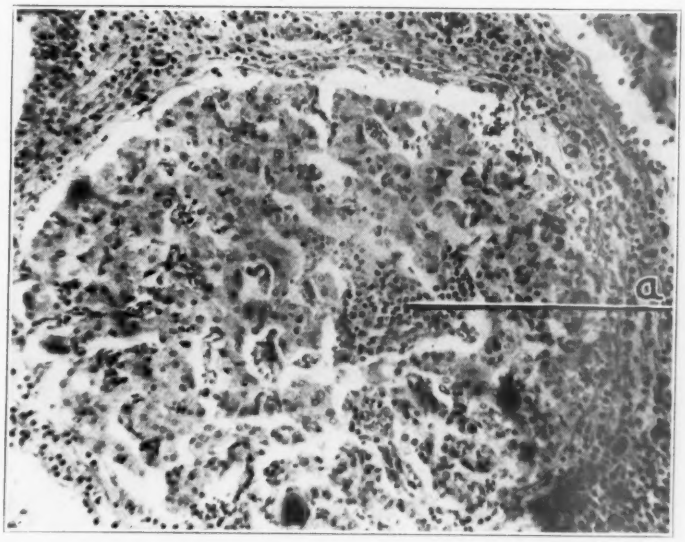

Fig. 2.—Low power photomicrograph (× 80) of an island of Langerhans. This island fills the entire field. Note the widened, cell-infiltrated peri-islet fibrous reticulum and the cellular infiltration of the islet itself (*a*).

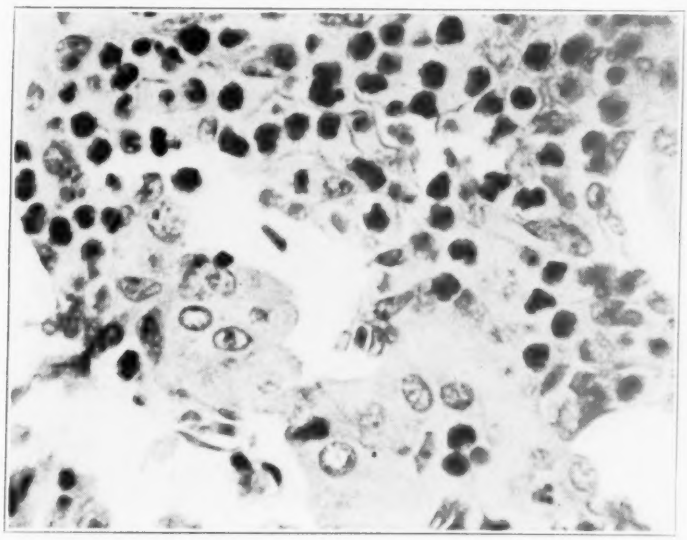

Fig. 3.—High power photomicrograph (× 400) of a portion of the islet in figure 2. Note the enlargement of the pale islet cord cells and the intravascular and extravascular infiltrating leukocytes (the dark-staining cells).

(table). The pathologic changes in the offspring have been limited to the pancreas, with two exceptions, in which adrenal hemorrhages were also present. The pancreas showed no gross changes. Histologically, an increase in the size and number of the islet cells was present in all cases, peri-insular edema and fibrosis in two cases (cases 2 and 10) and eosinophilic infiltration of the peri-islet, interlobular and intra-islet stroma in four cases (cases 7, 8, 9, 10). The hypertrophy of the islet has varied from 4 to 6 times normal (case 10) to 20 to 30 times normal (case 1).

It is generally believed that these fetal changes result from the hyperglycemic state of the mother, which, excessively stimulating the cells of the fetal islands, results in hypertrophy and hyperplasia. Holzbach [7] stated that the islands of Langerhans are capable of assuming functional activity early in fetal life. With the high maternal blood sugar removed at birth, the fetuses showing hypertrophied and hyperplastic islets presented a state of severe hypoglycemia. Indirect experimental evidence in support of these statements has been given by Carlson and Ginsburg [8] and Pack and Barber.[9]

The case of Feldmann [10] reported as one of hypertrophy of the fetal islet cells was not included in this series. Examination of his report led to the conclusion that the changes in his case were degenerative rather than proliferative and that they did not produce hyperinsulinism and hypoglycemia. Feldmann himself stated the belief that a toxin circulating in the blood stream produced degenerative changes in the pancreas of the mother and of the fetus, resulting in diabetes and the death of both.

Condition at Birth.—Of the ten infants whose cases are reviewed in this report, five were born prematurely and five at term. Each of the latter weighed 9 pounds (4,082 Gm.) or more at birth. Three of the premature infants were delivered by cesarean section.

New-born babies with diabetic mothers are, as a rule, large. This may be due to the fact that the fetus is supplied with excessive dextrose from the maternal blood. White [11] in her series found that 60 per cent of the babies born to diabetic mothers weighed over 8 pounds (3,624 Gm.). In 18 per cent of the cases collected by Skipper [5] the weight was over 10 pounds (4,536 Gm.).

Blood Sugar.—In all cases in which the blood sugar values were studied, hypoglycemia was found. It may be suggested that the hypo-

7. Holzbach, E.: Zentralbl. f. Gynäk. **53**:641 (March 16) 1929.
8. Carlson, A. J., and Ginsburg, H: Am. J. Physiol. **36**:217, 1914-1915.
9. Pack, G. T., and Barber, D.: Am. J. Physiol. **90**:466, 1929.
10. Feldmann, J.: Centralbl. f. allg. Path. u. path. Anat. **42**:435, 1928.
11. White, P.: Surg., Gynec. & Obst. **61**:324, 1935.

glycemia might have been the result of the adrenal hemorrhages.[12] It is, however, to be noted that in only two of the ten cases in this series were such hemorrhages found, while in all the cases there was hyperplasia of the islets. In the leading review of cases of adrenal hemorrhage [12] no mention was made of the pancreas or other organs. Furthermore, it is as yet highly doubtful whether an intimate association exists between the adrenal cortex or medulla and the pancreatic endocrine secretion in relation to the blood sugar level under conditions of endogenous body equilibrium,[13] although it has been suggested that destruction of the adrenal gland renders the body more sensitive to the effects of insulin.[14]

Clinical Course.—There were two stillbirths, two babies lived a few minutes after birth, others lived three, twelve, thirteen and fourteen hours, one lived four days and another lived thirty-two days. The child that lived four days presented at birth a normal, spontaneous cry and regular respiration. On the third day the child vomited portions of each feeding. On the fourth day the skin had a peculiar pasty color. The temperature was 38.3 C. (100.9 F.). That evening the infant was found dead. In case 10, as mentioned in the report, the patient had frequent bouts of cyanosis and collapse.

What are the signs of hypoglycemia in the new-born? Higgons [15] reported two cases of hypoglycemia in new-born infants in which the dominant signs were twitchings and convulsions. These findings were not present in our series of cases. Skipper [5] mentioned a 10 hour old infant with a blood sugar of 45 mg. per hundred cubic centimeters of blood but no other symptoms. Randall and Rynearson,[16] who reported the birth record of seven new-born infants with diabetic mothers, found hypoglycemia in most of the infants, but the dominant sign was cyanosis. In only one child were twitchings and mild convulsions present; in this infant the blood sugar values were normal.

Diagnosis.—The differential diagnosis between hypoglycemia in the new-born due to hyperinsulinism and hypoglycemia due to adrenal hemorrhage is difficult. In both conditions there may be an acute onset with the major signs of shock, followed by collapse and death within twenty-four hours. However, the clinical picture of adrenal hemorrhage in the new-born more commonly appears from thirty-six to seventy-

12. Goldzieher, M. A., and Gordon, M. B.: Endocrinology **16**:165, 1932.

13. Stewart, G. N., and Rogoff, J. M.: Am. J. Physiol. **65**:319, 1923.

14. Britton, S. W.; Geiling, E. M. K., and Calvery, H. O.: Am. J. Physiol. **84**:141, 1928.

15. Higgons, R. A.: Hypoglycemia in the New-Born, Am. J. Dis. Child. **50**: 162 (July) 1935.

16. Randall, L. M., and Rynearson, E. H.: Delivery and Care of New-Born Infant of Diabetic Mother, J. A. M. A. **107**:920 (Sept. 19) 1936.

two hours after birth, when it is noticed that the respirations are rapid and shallow with a rise of temperature to 104 F. or higher. A unilateral or bilateral tumor palpated in the region of the kidney aids in the diagnosis. Vomiting and convulsive seizures may also accompany this condition. Blood sugar values are low. The increasing accumulation of accurate determinations of blood sugar for infants with adrenal hemorrhage and for new-born infants with diabetic mothers may enable physicians to use the sugar level of the blood or the blood sugar tolerance curves [17] as a differential diagnostic feature. The importance of such differentiation and the therapeutic implications for the hypoglycemic state not of adrenal origin are obvious.

Any large baby that is difficult to resuscitate by aspiration and inhalation should have a determination of the blood sugar. With the Kramer-Gittleman modification of the Folin-Wu method,[18] this determination requires only a drop or two of capillary blood and is quite accurate. If the mother has had diabetes, a new-born child should be tested for hypoglycemia.

It is interesting to note the response of the child in case 10 to inhalation of oxygen and carbon dioxide as compared with that of an asphyxiated new-born infant suffering from cerebral edema or hemorrhage. An aid in the differential diagnosis of the two conditions may be found in their dissimilar responses to inhalation therapy. In cases of increased intracranial pressure, when resuscitation is accomplished it is usually with difficulty, and the sensorium and nervous impulses are depressed. The cry is cranial or whining, ocular changes are frequently present and the sucking reflex is poor or absent; if improvement in the cerebral condition occurs, it is a gradual process. In our case, once breathing was established the cry was strong, the sucking reflex good, and the eyes alert. After a short while the child would sink into coma, and stimulation would again be required.

Treatment.—Randall and Rynearson [16] recommended feeding a hypoglycemic new-born infant 10 cc. of a 10 per cent solution of dextrose by mouth, the dose to be given four hours after birth and every two hours for the next eight hours. This should be supplemented by inhalation of oxygen and carbon dioxide. While this therapy did not prevent death in our case, failure may have been due to our lack of persistence in the use of dextrose.

SUMMARY AND CONCLUSIONS

A case of hypoglycemia apparently due to hypertrophy and hyperplasia of the islands of Langerhans in a new-born infant is reported, and the literature reviewed.

17. Rascoff, H., and Jacobi, M.: To be published.
18. Orent, E. R.: J. Lab. & Clin. Med. **12**:435, 1927.

Determination of blood sugar should be made for all large new-born infants who do not respond to resuscitation or who are cyanotic and take feedings poorly.

If hypoglycemia is found in a new-born infant and the mother is not known to be diabetic, a sugar tolerance test should be made for her.

New-born infants that respond readily to inhalation of oxygen (O_2) and carbon dioxide only to sink into a coma shortly afterward should be suspected of having hypoglycemia. Such infants may respond to enterally or parenterally administered dextrose. It must be used persistently.

The relation of the concomitant adrenal hemorrhage present in two cases is briefly discussed.

MULTIPLE EPITHELIAL CYSTS OF ORAL MUCOUS MEMBRANE IN A NEW-BORN INFANT

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AND
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A white female infant with numerous raised gray nodules from 1 to 2 mm. in diameter studding the alveolar process of each jaw was observed in the service for the new-born of one of us (H. S.). The mother of the child, 24 years of age, had been in good health during pregnancy, and the delivery was normal. There

Fig. 1.—Labial view of the maxillary alveolar process at 8 days.

had been one previous pregnancy, with an abortion at two months. The oral condition of the infant was noted immediately after birth. The lesions (fig. 1) persisted throughout the neonatal period, which with the exception of a mild irritation of the skin was uneventful.

On the fourteenth day a small piece of tissue including one of the nodules was removed from the mucous membrane over the alveolar process in the region of the right upper temporary cuspid crypt. The tissue was fixed in a 10 per cent dilution of solution of formaldehyde U. S. P., embedded in pyroxylin (celloidin), cut serially and stained with hematoxylin and eosin. Microscopic examination of the sections revealed several epithelial cysts of various sizes. There appeared to be a rupture of the largest cyst through the surface epithelium. This may have been either

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spontaneous or caused by the trauma of the removal of tissue for biopsy. One smaller cyst showed a similar opening. The structures were lined with stratified squamous epithelium similar to that of the oral mucosa and were filled with cellular débris, blood cellular elements and a homogeneous substance taking a blue stain. There were no evidences of glands in any of the sections. The superficial layers

Fig. 2.—Low power photomicrograph of tissue removed at 14 days, showing a collapsed cyst.

of the epithelial lining revealed a greater degree of degeneration than similar portions of the surface epithelium (fig. 2).

The serial sections showed a continuity of the cyst lining with the basal layer of the oral epithelium. This suggested that the cyst formation might have been due to the isolation or semi-isolation of the deeper epithelial cells by the rapid proliferation of underlying connective tissue (fig. 3). The growth of both

epithelial and connective tissue is extremely rapid in new-born infants, and segregation of a few active epithelial cells might well produce epithelial cysts. It is suggested that central degeneration produces the cyst, which extends along the cord, approaching or reaching the surface epithelium; and that the lumen widens in the direction of the oral cavity and eventually ruptures externally, when the cyst collapses. A means for spontaneous resolution is provided in this way.

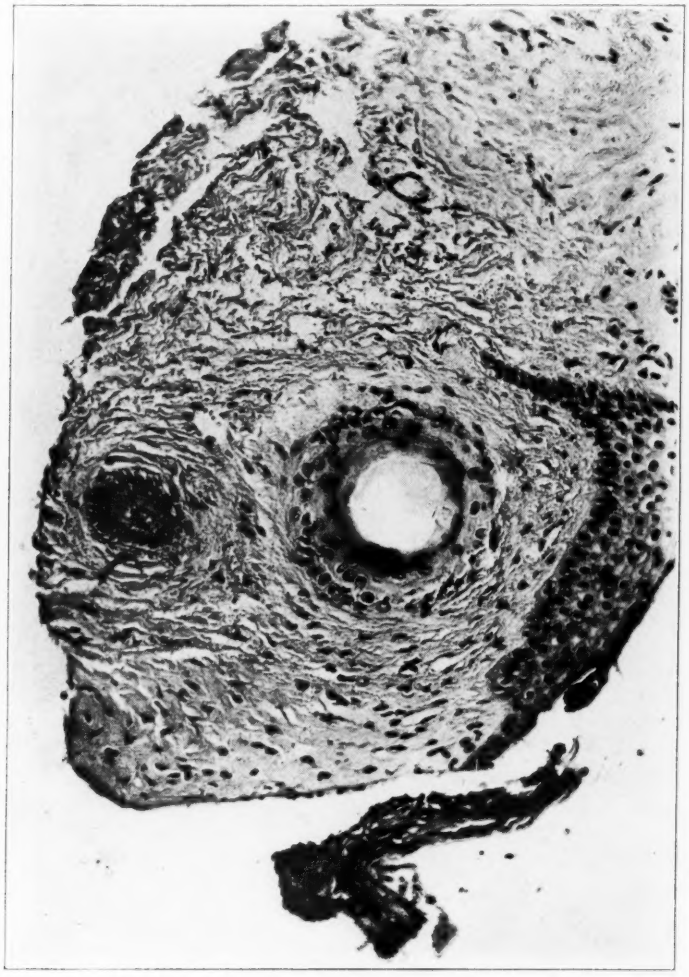

Fig. 3.—High power photomicrograph of tissue removed at 14 days, showing a small cyst.

Observation of the infant at 7 months of age revealed only a few remaining nodules over the labial portion of the crypts of the upper deciduous cuspid teeth. The mucous membrane of the lower jaw was normal, and the two lower central incisors had erupted. No treatment was instituted.

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MORQUIO'S DISEASE

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Morquio in 1929 described two cases of familial and generalized osseous dystrophy, similar in many features to previously reported cases of achondroplasia, or chondro-osteodystrophy, yet impressing one as involving a separate syndrome. The condition is generally considered to be osteochondropathy sui generis. In 1935 Morquio added to the two cases already reported the detailed clinical histories of two more of the affected brothers in the same family of five. He could add little that was new to his original classic description of the peculiar and rare clinical syndrome.

Morquio wrote in 1929:

The children are born normal and develop normally during the first year. When they start walking, changes are noted, and these become accentuated in the following months and become stationary and definite. These manifestations are bony changes, without any pain, which affect the body, the vertebral column and the extremities and spare the head and the face. Functional troubles result, especially those of motility, and physical troubles modify completely the harmony of the body..

The deformities of the skeleton are generalized and absolutely symmetrical. In certain regions there are bony protuberances, as in the sternum, the vertebral column, the epiphyses of the shoulder, the elbows, the knees, etc. In others there is retardation or absence of ossification, particularly in the palm, where one finds a complete void. The ligaments, and particularly the muscles, are soft and relaxed, which gives a peculiar flaccidity to the joints, limited, however, in certain regions, as in the shoulders and the elbows, by bony deformities. In others, however, as in the hands and the feet, this flaccidity reaches extreme degrees.

As a consequence, the whole body presents a marked deformity, characterized by longitudinal shortening and an anteroposterior deepening of the thorax, with the sternum projecting to a point, this forming a contrast with the extremities, which, though deformed, have normal dimensions, and giving to the children the appearance of sufferers from Pott's disease with an extensive cicatricial gibbus.

The genu valgum, the flat foot, the malformation of the vertebral column and the weakness of the muscles and the tendons give rise to a difficult gait resembling that of a duck. The strength in the hands and the feet is greatly diminished, without apparent muscular atrophy or any change in the electrical reaction. The mentality is normal, and the children have intelligent facial expressions.

From the Woman's General Hospital, Montreal, Canada.

Roentgenologic studies show profound alteration in osteogenesis, explicable by the great diminution of the calcium in the blood. These characteristic changes are rarefactions, malformations, destructions, retardations and absences, more or less complete, affecting particularly the epiphyses of all long bones, big and little, of the extremities.

Fig. 1.—Photograph of the patient at the age of 10 years, showing the dwarfed stature, the large, square head on a short neck, the disproportionate elongation of the upper extremities, knock knee, flatfoot and kyphosis.

The disease seems to take a progressive, though very slow, course; the cartilages ossify, but the decalcification and the osteochondritis become more accentuated.

Fig. 2.—Roentgenogram of the hands, showing generalized decalcification. The ragged, irregular, mottled distal ends of the radius and the ulna are bilaterally and symmetrically broadened. Carpal ossification has been delayed, that present corresponding to that of a child of only 7 years.

Fig. 3.—Roentgenogram of the feet, showing generalized decalcification, slightly delayed tarsal ossification, changes at the distal ends of the tibia and the fibula similar to those observed at the distal ends of the radius and the ulna. (See figure 6 for lateral view.)

Fig. 4.—Roentgenograms of the upper extremities, showing lateral views of both forearms, elbows and wrists, characteristic bony changes of the distal ends of the radius and the ulna as in figure 2 and delayed osseous development in the elbows.

Since Morquio's publication a few similar cases have been reported and identified by various authors with the instances of Morquio's syndrome.

Valentin in 1930 reported two cases of a condition which he separated as a familial multiple osteochondropathy from the typical chondrodystrophy. Ruggles encountered since 1918 eight cases of peculiar

Fig. 5.—Anteroposterior roentgenogram of the lower extremities, showing a markedly ragged appearance of the distal femoral epiphyses, a prominent median femoral condyle and a bony defect in the lateral condyle. The fibulas are shortened.

dwarfism—five of them in one family—and published them in 1931. Meyer and Brennemann in 1932 reported one case, that of a boy of 8 years whom they had observed since he was 8 months old. Further cases were reported by Coward and Nemir (two brothers), by Barnett (two brothers) and by Brown (two brothers and their mother) in 1933;

by Davis and Currier (two brothers) and by Sainz de los Terreros and Lacalle (one case) in 1934; by Giraud and Bert (two brothers) in 1935, and by Summerfeldt and Brown (two brothers) in 1936. The cases of Davis and Currier were the only ones in which changes in the skull were observed.

Fig. 6.—Lateral roentgenograms of the lower extremities, more clearly visualizing the changes observed in figure 5. Moderate anterior bowing of the tibia and the fibula can be seen.

All together *27* cases of Morquio's disease have been reported up to the present time. A few cases of a similar and possibly identical condition were described prior to Morquio's publication, but these were classified by their authors as instances of atypical chondrodystrophy or multiple osteochondropathy (Silfverskiöld, Grudzinski, Brailsford, Campbell, Dale, Buxton and others).

REPORT OF A CASE

I. V., a girl 10 years old, was admitted to the hospital for acute tonsillitis. There was a history of whooping cough and possible rickets at 3 years. She started walking before she was 2 years old; she grew only a little every year. Her sisters and brothers—there were ten children in the family—were physically normal, as were her parents, according to information acquired indirectly. The child was mentally normal but suffered from headaches at school. Her physical

Fig. 7.—Roentgenogram of the pelvis and the hip joints, showing delayed osseous development, small, irregular, mottled femoral epiphyses and a shortened femoral neck.

appearance was characteristic (fig. 1). There was marked shortening of the trunk and the child's arms reached nearly to her knees. There were marked kyphosis in the dorsolumbar region and a pigeon breast with Harrison's groove. The head was on a short neck and appeared larger than normal and prominent in front, with the eyes spaced widely and showing signs of a previous mild chorioretinitis; the root of the nose was somewhat depressed. The teeth did not show signs of rickets.

In the standing position the child appeared distinctly knock kneed and flat footed, and in walking there was a marked waddling gait. The muscles were flabby, but no abnormal flexibility of the joints was noticeable.

Most of the measurements were below the minimum for her age, the circumference of her head being 20¾ inches, or 52.7 cm. (normal, 20 7/10 inches, or

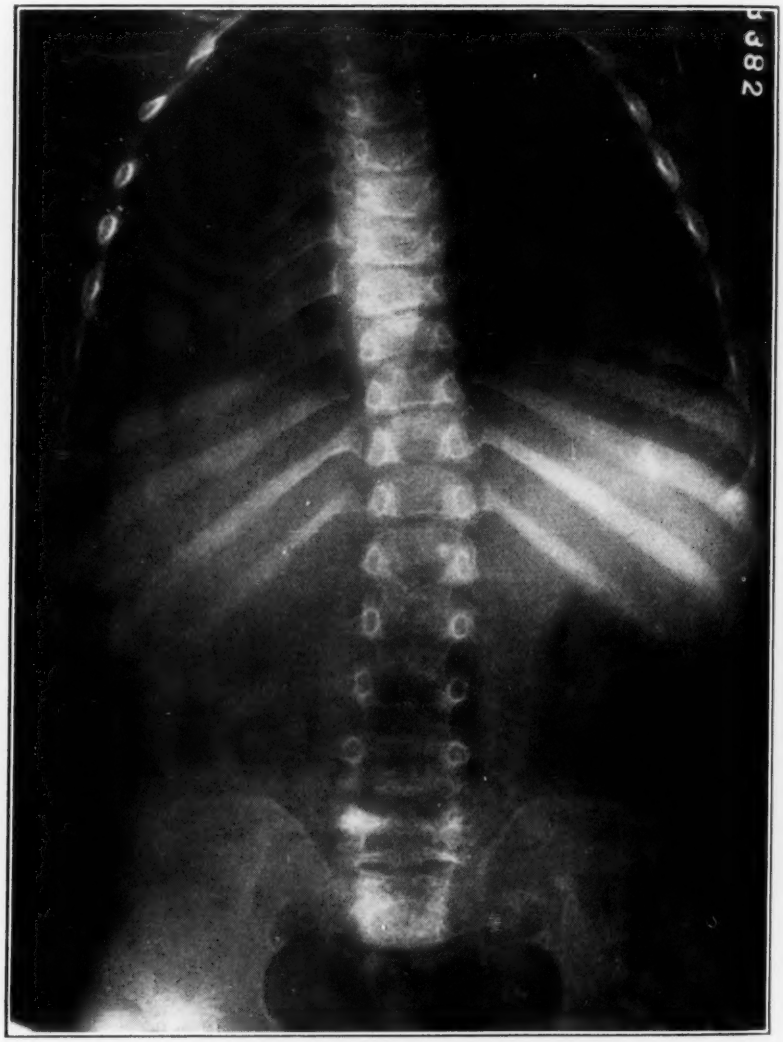

Fig. 8.—Anteroposterior roentgenogram of the dorsolumbar portion of the spine, showing moderate scoliosis and heavy, broadened ribs.

52.6 cm), the circumference of the chest, 21¾ inches, or 55.1 cm. (normal, 25 inches, 63.5 cm.), height, 34 inches, or 86.4 cm. (normal, from 51⅕ to 54⅘ inches, or 130 to 139 cm.) and weight, 35 pounds (15.9 Kg.) (normal from 56⅕ to 71 pounds, or 25.5 to 32.2 Kg.).

Clinical and laboratory findings were as follows: Urinalysis, the Wassermann test of the blood and the Mantoux test gave negative results. The basal metabolic rate was + 61.5 per cent on January 28, + 36 per cent on February 1 and + 42 per cent on February 7. Results of the sugar tolerance test were low, the sugar

Fig. 9.—Lateral roentgenogram of the dorsolumbar portion of the spine, showing moderate kyphosis. The vertebral bodies are wide and flat; some are pointed anteriorly and are ragged. The intervertebral disks appear as thick as the bodies.

content of the blood being, when the patient was fasting, 104 mg., one hour after a test meal, 114 mg., and two hours after a test meal, 160 mg., per hundred cubic centimeters. The fluid output averaged about half the intake.

Chemical analysis of the blood showed per hundred cubic centimeters: calcium (serum), 10.6 mg.; phosphorus (serum), 5 mg.; urea nitrogen, 20 mg.; creatinine 1.7 mg.; chlorides, as sodium chloride (plasma), 578 mg., and cholesterol, 143 mg.

The roentgenologic examination (figs. 2 to 11) showed characteristic malformation.

A generalized decalcification of the skeleton was noticed. The distal ends of the diaphyses of the radius and the ulna, and to a slighter degree of the tibia and

Fig. 10.—Postero-anterior roentgenogram of the skull shows it to be square and relatively large.

the fibula, were broadened, irregular and ragged and had dense, mottled depositions of calcium. These changes were still more striking in the distal femoral epiphysis, which showed a large ragged bony defect in the posterior and the lateral portion of the outer femoral condyle. The median femoral condyle was prominent, which accounted for the knock knee. The fibula was shortened, and the head lay below its normal position. All these changes were generalized and symmetrical.

The pelvis was broadened, with large acetabular cavities, a small irregular mottled epiphysis and a shortened femoral neck. There was no union between the ischium and the pubis, indicating an osseous development equal to that of the average 7 year old child.

There were moderate scoliosis and kyphosis in the dorsolumbar portion of the spine. The vertebral bodies were wide and flat, and some were pointed anteriorly and ragged. The intervertebral disks were as thick as the bodies. The ribs were heavy and broadened at the costal cartilages.

Fig. 11.—Lateral roentgenogram of the skull shows no evidence of pathologic bony changes. The sella turcica is small.

The carpal bones were smaller than normal; the distal epiphysis of the ulna had appeared, and the pisiform bone was still absent. Carpal ossification corresponded to that of a normal child of about 7 years. The tarsal bones were fairly well developed and regularly outlined. The bases of the metacarpal and metatarsal bones were not pointed, although other authors have reported observing that trait.

The elbows showed development only of the centers of ossification of the capitulum humeri and the proximal radial epiphysis, this condition corresponding to that normally found in children aged about 5 or 6 years.

The skull was free and the sella turcica normal. There was no evidence of pulmonary or cardiac change.

COMMENT

A single case has been presented, after a critical review of the literature, of a condition apparently identical with the clinical syndrome of Morquio's disease.

The patient showed many of the characteristic features described by Morquio, though to a less marked degree than the photographs and the description of Morquio's cases, as quoted above, would indicate.

Clinically, there were present dwarfism, kyphosis, genu valgum, pes planus, muscular flabbiness and certain ocular symptoms.

Roentgenologically, generalized and symmetrical osseous changes were noticeable: decalcification, deformity and destruction of epiphyses, delayed osseous development, peculiar appearance of the ends of the diaphyses of the long bones, typical changes of the vertebrae and shortening of the fibulas. No pathologic changes were evident in the skull.

Other features observed by Morquio, however, were absent in this case. No definite evidence of a familial tendency could be ascertained from the available information. The calcium metabolism was normal and could not be held to account for the profound disturbance in the osteogenesis, as was considered possible in Morquio's cases.

Another theory of Morquio was that the underlying mechanism may be an intervention of the nervous system directly or by way of the endocrine system. There is possibly an underlying endocrine or metabolic disturbance interfering with the normal development of the epiphyses and delaying the appearance of the centers of ossification. However, no results were obtained from administration of pituitary, thyroid and other glandular extracts, or after medication with calcium or viosterol.

Another explanation as to the etiology of this condition has been given recently by Giraud and Bert. They expressed the opinion that Morquio's disease is an arthroligamentary dystrophy, a clinical syndrome of greatly deforming dystrophic hyperlaxity of the ligamentary apparatus.

According to this theory, the weakness of the ligamentary apparatus and, as an accessory, the weakened resistance of the skeleton are the primary and primordial cause of Morquio's disease. Under the influence of the upright position and after walking, a vertical sinking in of the skeleton occurs, resulting in faulty positions, due to luxation and subluxation, which are at first reducible but finally become permanent and lead to permanent osteo-arthritic deformities.

Nosologically, Giraud and Bert classified Morquio's disease on the basis of a familial mesodermal dysplasia, in the same group with the

syndrome of Lobstein, Oppenheim's disease and the syndrome of Danlos and Ehlers.

The relation between achondroplasia of Parrot and Morquio's disease has been much under discussion, though the differentiation even between atypical achondroplasia, the formes frustes and Morquio's disease is clinically not difficult and roentgenologically obvious.

Other authors have classified Morquio's disease as one of the several types of osteochondrodystrophy. It seems that the general opinion held today is that Morquio's disease is an independent, generalized and familial osteochondropathy.

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Progress in Pediatrics

PATHOLOGIC BACKGROUND OF CEREBRAL DIPLEGIA

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The problem of the cerebral birth palsies remains in a state of confusion, despite the many investigations on the subject. One reason lies in the fact that not enough cognizance has been taken of the probability that there are many different causes and pathologic substrata for conditions which appear clinically similar. Another reason is that it has been extremely difficult to discriminate between congenital and acquired lesions in many cases of early involvement. Finally, there has frequently been confusion between cause and lesion; this has resulted in an effort to assign to a single clinical group a single cause.

For this reason we have chosen to study the cerebral diplegias as representing a unit in the entire group of cerebral birth palsies, hoping at least to clarify thereby the pathologic background of such conditions and possibly at the same time to indicate the etiologic factors in some instances.

A study of cerebral birth palsies logically should include a study of cerebral diplegia, infantile hemiplegias, both unilateral and bilateral, paraplegias, choreo-athetosis with or without hemiplegias, double athetosis and probably also the cerebellar type of diplegia. It is obvious from a mere recital of these various disorders that they include a wide variety of conditions, with a varied background and undoubtedly a varied etiology. They include also both congenital and acquired conditions, though this in itself is not a valid reason for consideration of both congenital and acquired states in the same group. Exemplifying the conditions cited are instances of late infantile hemiplegia which has resulted from encephalomyelitis or embolism. No useful purpose could be served by a consideration of this group of cases with one in which

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involvement occurs at or near birth, because the conditions of development are, without doubt, very different in the two groups. Indeed, some of the confusion in the problem of the cerebral birth palsies has resulted from indiscriminate grouping of cases of late infantile hemiplegia with other cases of a different type from the whole field of the cerebral birth palsies. Similarly, cases of double hemiplegia should be excluded from study because the conditions of development of this disorder are frequently similar to those of the late infantile type.

We have tried to record all the cases of cerebral diplegia in which pathologic studies were made. By this means we should at least have all the facts at our command from which to draw conclusions concerning the pathologic, and possibly the etiologic, background of cerebral diplegia. During the course of our study many more references than those recorded were covered, but since only pathologically verified cases were wanted, it was necessary to exclude many valuable clinical studies. Our study is therefore presumably complete for verified cases of cerebral diplegia, but not for the entire subject.

CLASSIFICATION

What should be included in a study of cerebral diplegia? Strictly speaking, there should be admitted only cases of diplegia in which there were characteristic signs, such as greater involvement of the legs than the arms, predominance of spasticity over weakness and relative escape of the face. It has become customary, however, to include in the cerebral diplegias (1) cerebral diplegia proper, (2) bilateral hemiplegias, (3) paraplegias and (4) choreo-athetosis. Freud,[1] for example, included (1) generalized cerebral rigidity, (2) spastic paraplegia, (3) bilateral hemiplegia and (4) generalized chorea and bilateral athetosis. Osler [2] included (1) spastic rigidity of the new-born (Little's disease) and (2) bilateral spastic hemiplegia. Sachs and Petersen [3] included (1) cerebral diplegia, (2) paraplegias and (3) hemiplegias. Ironsides [4] suggested the following grouping of cerebral diplegias: (1) cortical types—(*a*) spastic paraplegia and (*b*) spastic diplegia; (2) striatal types—(*a*) bilateral chorea and (*b*) bilateral athetosis; (3) cortical-striatal types; (4) cerebrocerebellar types.

1. Freud, S.: Die infantile Cerebrallähmung, in Nothnagel, H.: Specielle Pathologie und Therapie, Vienna, A. Hölder, 1897, vol. 9, pt. 3.

2. Osler, W.: Cerebral Palsies of Children, Philadelphia, P. Blakiston's Son & Co., 1889.

3. Sachs, B., and Petersen, F.: A Study of Cerebral Palsies of Early Life Based upon an Analysis of One Hundred and Forty Cases, J. Nerv. & Ment. Dis. **15**:295, 1890.

4. Ironsides, R.: Cerebral Diplegia: Its Classification and Prognosis, Proc. Roy. Soc. Med. **25**:578, 1932.

The classifications hitherto proposed for cerebral diplegia are chiefly clinical. Any effort to establish an etiologic classification is doomed to failure because of the numerous factors which may be responsible for this condition. Similarly, a pathologic classification is untenable because of the varied pathologic background. A clinical grouping is therefore necessary, despite all its shortcomings. We propose the following grouping of the diplegias:

1. Cerebral diplgeia (Little's disease). This is the type originally described by Little; it needs no further comment to justify its inclusion.

2. Spastic paraplegia. This type of paralysis is probably an incomplete form of diplegia and is universally accepted as part of the diplegia group. Freud pointed out, in fact, that there are all sorts of transitions in this group, from partial involvement of the arms to complete generalized spasticity. He noted also that in occasional cases there is at first a generalized spastic condition, which later becomes spastic paraplegia. In any event, pure paraplegia is probably less common than conditions in which the legs are predominantly involved and the arms are less affected.

3. Bilateral choreo-athetosis and double athetosis.

4. Cerebellar type of diplegia.

The bilateral hemiplegias have not been included because they appear late and because, as Dejerine [5] pointed out, they are clinically different from the true diplegias. In bilateral hemiplegia the arms are more affected than the legs, facial involvement is more pronounced and there is usually a greater degree of paralysis of both the arms and the legs than in cerebral diplegia. While there are probably a great many transitional forms between bilateral hemiplegia and true cerebral diplegia, it has seemed to us desirable to exclude bilateral hemiplegia from the group of cerebral diplegias.

PATHOLOGICALLY VERIFIED CASES OF CEREBRAL DIPLEGIA

Cerebral Diplegia.—Much has been written on the clinical features of cerebral diplegia, and there has been a great deal of speculation on the pathogenesis of the condition. Proportionately little space has been devoted to the pathologic basis of the disease. It is obvious, however, that before one speculates on the causes and pathogenesis of the lesions in cerebral diplegia one should be informed on the actual lesions in the brain.

In a study of the pathologically verified cases, the fact stands out clearly that a variety of lesions have been described in typical cases of

5. Dejerine, J.: Maladie de Little, Rev. mens. d. mal. de l'enf. **10**:153, 1892.

cerebral diplegia. Indeed, the very diversity of the lesions gives some clue to the possible pathogenesis of the condition. An early report, and still one of the best, is that of Sachs and Petersen (1890), who made a thorough study of the lesions. Of twenty-four cases of cerebral diplegia, they observed atrophy, sclerosis or cysts in nineteen, porencephaly in four and cerebral agenesis in one. The exact details of the anatomic lesions in these cases were not recorded, but the types of lesions were such as to make no detailed dsecription necessary. In twenty-two of their twenty-four cases of diplegia, the condition was congenital.

Freud recorded a number of causes of cerebral diplegia. He divided them into intra-uterine, natal and extra-uterine. He recorded the following lesions: porencephaly, developmental inhibition of the pyramidal tracts, cortical agenesis, meningeal hemorrhage, chronic meningoencephalitis, scleroses, cysts, partial atrophy, hemorrhage, thrombosis and embolism and acute polio-encephalitis of Strümpell. A mere recital of these conditions serves to impress the fact that many types of lesions are responsible for the condition known as cerebral diplegia. The significance of these various lesions will be reserved for later discussion.

Jakob,[6] whose approach to these problems was through the more modern trends in neuropathology, included among the diplegias: status marmoratus (Vogt) and status dysmyelinatus of the pallidum (Vogt). In addition, other lesions, similar to those recorded by Sachs and Petersen and by Freud, have been reported.

Osler's studies on bilateral spastic hemiplegia in children revealed a similar diversity of pathologic conditions. He recorded the following types of lesions: porencephaly, partial cerebral atrophies, general cortical sclerosis and extreme atrophy of both cerebral hemispheres. These conditions were similar to those recorded by others. Long-Landry[7] noted the following types of lesions, in cases of cerebral diplegia: cerebral agenesis, porencephaly, cerebral atrophy or sclerosis, microgyria, cerebral cysts, diffuse meningitis and hemorrhagic pachymeningitis. Campbell,[8] in one of his earlier contributions, reported diffuse symmetrical atrophy of both cerebral hemispheres, with destruction of the nerve cells and neuroglial proliferation. Sometimes the pyramidal tracts are absent in such cases. Campbell stated that porencephaly was sometimes encountered, but more commonly with double hemiplegia

6. Jakob, A.: The Anatomy, Clinical Syndromes and Physiology of the Extrapyramidal System, Arch. Neurol. & Psychiat. **13**:596 (May) 1925.

7. Long-Landry, M.: La maladie de Little; étude anatomique et pathogénique, Thèse de Paris, no. 252, 1911.

8. Campbell, A. W.: Cerebral Sclerosis, Brain **28**:367, 1905.

than with diplegia. Hammarberg[9] observed severe disturbances in cerebral development in nine cases of idiocy associated with cerebral diplegia. In each of these cases the brain was defective and showed a developmental stage far below the chronological age of the patient. In four cases in which there were severe amentia and spastic paralysis, the brain showed only one layer of cortical cells, resembling in structure that of a 5 month fetus. In two cases typical Betz cells were lacking in the motor cortex. In Ross'[10] case there were absence of the Betz cells in the precentral gyrus and atrophy in the region of the sylvian fissure. An example of extensive agenesis was noted in the case reported by Binswanger.[11] In this case the brain was very small, and most portions were absent, except a part of the central gyri. There were atrophy of the thalamus, agenesis of the corpus callosum and degeneration of the corticospinal tracts. Similarly, in the case of Anton[12] only the temporal lobes were more or less intact; the rest of the cortex was atrophied. The white matter was much decreased in amount, and the entire corticospinal system was rudimentary. On the other hand, in the case of Dejerine and Sollier[13] there were only atrophy of the "posterior lobe" and an abnormal appearance of the frontal convolutions. In the case of Muratoff[14] there was complete atrophy of the Betz cells, with thinning and atrophy of the fibers in the corticospinal tract. The anterior horn cells were atrophied. Mya and Levi[15] reported aplasia of the Betz cells. Rolly[16] also observed atrophy or degeneration of the Betz cells and similar lesions in the anterior horn cells. Long-Landry noted diffuse inflammatory lesions in four cases of cerebral diplegia. These were accompanied in one case by bilateral porencephaly and in the others by disturbances in the corticospinal system. Ford,[17] in a study of six cases of cerebral diplegia, divided the

9. Hammarberg, C.: Studien über Klinik und Pathologie der Idiotie, translated by Walter Berger, Upsala, E. Berling, 1895.

10. Ross, J.: On the Spasmodic Paralysis of Infancy, Practitioner **29**: 344 and 473, 1882.

11. Binswanger, O.: Ueber eine Missbildung des Gehirns, Virchows Arch. f. path. Anat. **87**:427, 1882.

12. Anton, G.: Ueber angeborene Erkrankungen des Centralnervensystems, Vienna, A. Hölder, 1890.

13. Dejerine, J., and Sollier, P.: Premier cas d'autopsie d'athétose double datant de la première enfance, Bull. Soc. anat. de Paris **63**:601, 1888.

14. Muratoff, W.: Zur Kenntnis der verscheidenen Formen der diplegischer Paralyse, Deutsche Ztschr. f. Nervenh. **7**:84, 1895.

15. Mya, G., and Levi, G.: Studio clinico e anatomico relativo ad un caso di diplegia spastica congenita (Morbo di Little), Riv. di pat. nerv. **1**:417, 1896.

16. Rolly: Angeborene doppelseitige Starre (Little'sche Krankheit) bei Zwillingen mit Sektionsbefund, Deutsche Ztschr. f. Nervenh. **20**:152, 1901.

17. Ford, F. R.: Cerebral Birth Injuries, Medicine **5**:121, 1926.

lesions responsible for the condition into three main groups: (1) atrophic lobar sclerosis, which he found to be by far the most frequent lesion, (2) developmental defects in the pyramidal tracts and (3) status marmoratus (Vogt).

The study of MacNutt [18] on the occurrence of meningeal hemorrhage and its responsibility for cerebral diplegia is well known. She reported a case of bilateral infantile spastic hemiplegia in a child of 2½ years in which gross examination showed atrophy of both ascending frontal convolutions. The microscopic study of Dr. William H. Welch revealed bilateral atrophy of the paracentral lobule, the precentral gyrus and the posterior portions of the first, second and third frontal gyri. The atrophy was most marked in the paracentral lobule, the anterior portion of the central gyrus and the upper two thirds of the postcentral gyrus. The cortex in these areas was replaced by a fibrillary scar; Betz cells were not seen, and there was secondary degeneration of the pyramidal tracts. The anatomic diagnosis was sclerosis of the greater part of the motor cortical area of both cerebral hemispheres. MacNutt concluded that meningeal hemorrhage at the time of birth was responsible for the clinical picture in her cases and that the resulting atrophy of the brain in the case just cited was secondary to the meningeal hemorrhage. This case was the only one in which she recorded necropsy observations.

Norman [19] recently recorded a well studied case of cerebral diplegia in a child of 5 years. The brain showed atrophy of the upper half of the left precentral gyrus, the upper third of the left postcentral gyrus and the left superior parietal lobule. The right hemisphere was grossly less affected than the left. Microscopic study revealed fibrosis of the pia-arachnoid over the cortex. In the cortex itself was extensive loss of nerve cells, most marked in the atrophic gyri. Both paracentral lobules showed loss of ganglion cells in laminae III and V. In the precentral gyrus the loss was most pronounced in lamina III. There were similar lesions in the left postcentral gyrus and the superior parietal lobules, except that in these areas the internal granular layer was most affected. Less extensive defects were noted in the frontal, temporal and occipital areas. There was severe sclerosis in the paracentral lobules, the upper portions of the precentral and postcentral gyri and the subjacent white matter. This was due chiefly to increase in the number of astrocytes. The radial and supraradial fibers were poorly represented in the affected areas.

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18. MacNutt, Sarah: Double Infantile Spastic Hemiplegia, Am. J. M. Sc. **89**:58, 1885; Seven Cases of Infantile Spastic Hemiplegia, Arch. Pediat. **2**: 20, 1885.

19. Norman, R. M.: Bilateral Atrophic Lobar Sclerosis Following Thrombosis of the Superior Longitudinal Sinus, J. Neurol. & Psychopath. **17**:135, 1936.

In the basal ganglions, the thalamus showed intense gliosis and decrease in the number of ganglion cells; the putamen revealed marked gliosis and loss of cells, and the pallidum was normal. The cerebellum showed loss of Purkinje cells. In the pyramidal system the Betz cells were reduced in number; the pyramids in the medulla were smaller than normal, with thinning of the myelinated fibers and excess of neuroglia, and the lateral spinal columns showed loss of myelin and glial hyperplasia. Norman regarded the atrophic lobar sclerosis as due to a degenerative process resulting from obstruction of the superior longitudinal sinus.

In a small number of cases there has been little or nothing to explain the finding of cerebral diplegia. Thus, in three cases of cerebral diplegia described by Ganghofner [20] the brain was normal, both grossly and microscopically. In three cases reported by Spiller [21] there was nothing in the condition of the corticospinal tracts to explain the spastic diplegia. In two cases the Betz cells were normal in number, and in another they were slightly reduced. The pyramidal tracts in the spinal cord were not degenerated. In one of the cases the fibers of the pyramidal tracts were abnormally fine and appeared to be of imperfect development. Similar cases were recorded by Binswanger, Gierlich [22] and Ford. Railton [23] noted in his case normal pyramidal tracts and diminution in the number of Betz cells. Cestan [24] (cases 31, 32, 33, 35 and 37) observed an essentially normal corticospinal system, slight atrophy of the pyramidal tract and its fibers on one side (case 30) and slight sclerosis of the corticospinal tracts (case 36). Similarly, Anglade and Jacquin [25] noted no corticospinal lesions in their case. Wachsmuth [26] saw only slight atrophy of the left pyramidal tract. The changes in the pyramidal tracts in spastic paraplegia were classified by Rhein [27] as follows:

1. Fineness of fibers of the pyramidal tracts (Spiller; Binswanger).
2. Scarcity of pyramidal fibers (Ganghofner; Gierlich).

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20. Ganghofner, F.: Ueber cerebrale spastische Lähmungen im Kindesalter, Jahrb. f. Kinderh. **40**:219, 1895.

21. Spiller, W. G.:: On Arrested Development and Little's Disease, J. Nerv. & Ment. Dis. **25**:81, 1898.

22. Gierlich, N.: Ueber secundäre Degeneration bei cerebraler Kinderlähmung, Arch. f. Psychiat. **23**:201, 1891.

23. Railton, T. C.: Birth Palsy, Brit. M. J. **1**:441 (Feb. 27) 1882.

24. Cestan, R.: Le syndrôme de Little; sa valeur nosologique, sa pathologie, Thèse de Paris, no. 328, 1889.

25. Anglade and Jacquin: Syndrôme de Little, Encéphale **4**:252, 1909.

26. Wachsmuth, H.: Cerebral Kinderlähmung und Idiotie, Arch. f. Psychiat. **34**:787, 1901.

27. Rhein, J. H. W.: Spastic Paraplegia Dating from Childhood with Little or No Demonstrable Lesion in the Pyramidal Tracts, Am. J. M. Sc. **138**:885, 1909.

3. Incomplete myelination without diminution in the number and size of the fibers.
4. Agenesis or imperfect development of the pyramidal tracts.
5. Atrophy of the pyramidal tracts.

Before we dismiss the subject of the pathologic picture in the true diplegias, we should mention a group of cases which at one time assumed great importance in a discussion of cerebral diplegia. These are the cases of polio-encephalitis described by Strümpell. In 1885 Strümpell [28] reported twenty-four cases of hemiplegia, monoplegia, epilepsy and athetosis in which he stated that the paralysis was due to polio-encephalitis. He had no pathologic studies to support his contention, but his concept found a ready reception, and his report was followed by numerous contributions. These included purely clinical studies by Heine,[29] Kast,[30] Wolfenden,[31] Handford [32] and Ranke.[33] The only pathologic study of this subject was made by Wallenberg,[34] who up to 1886 reported forty-eight cases of Strümpell's type of polio-encephalitis. Twelve of the patients died soon after onset of the paralysis. In four instances there was embolism of the middle cerebral artery; in three, probable embolism of this artery, and in five hemorrhage into the cerebral hemispheres or the ventricles. In thirteen other cases there were atrophy and sclerosis of different parts of the brain. In only three cases was polio-encephalitis a possible cause, and one might regard with skepticism the concept that the thickening of the meninges, the softenings and the porencephalic defects were the residual effects of polio-encephalitis. In any event, Wallenberg determined that the lesions in Strümpell's type of polio-encephalitis were due to many causes and only infrequently to polio-encephalitis itself.

We emphasize this aspect of the problem of diplegia because even today polio-encephalitis is assigned as one of the causes of lesions in the diplegia group. Actually, Strümpell's cases should be discarded. In all of them the disease was infantile or late infantile hemiplegia, and in most instances it would be regarded today as encephalomyelitis

28. von Strümpell, A.: Ueber die akute Encephalitis des Kindes, Jahrb. f. Kinderh. **22**:173, 1885.

29. Heine: Ueber cerebrale Kinderlähmung, München. med Wchnschr. **33**: 293 (April 27); 315 (May 4) 1886.

30. Kast, A.: Zur Anatomie der cerebralen Kinderlähmung, Arch. f. Psychiat. **18**:280, 1887.

31. Wolfenden, R. N.: On Infantile Cerebral Paralysis, Practitioner **37**:161, 1886.

32. Handford, H.: On Cerebral Infantile Paralysis, Brain **9**:265, 1886.

33. Ranke, H.: Ueber cerebrale Kinderlähmung, Jahrb. f. Kinderh. **24**:78, 1886.

34. Wallenberg, A.: Ein Beitrag zur Lehre von den cerebralen Kinderlähmungen, Jahrb. f. Kinderh. **24**:384, 1886.

of virus origin, secondary to the various exanthems or to other causes. We believe, therefore, that the polio-encephalitis of Strümpell should not be regarded as a cause of cerebral diplegia, and we have not included any such cases in our group.

Congenital Double Athetosis.—In some cases of cerebral diplegia there has been observed the status marmoratus of the Vogts.[35] This is associated with a clinical picture of athetosis, rigidity and epileptic seizures (Jakob). In addition, mental retardation and mental deficiency are frequently present. In such cases there are in the striatum large numbers of fine, delicate myelinated fibers, with destruction of large parts of the striatum and replacement by neuroglia. Because of the marbled appearance of the brain in these cases, the term status marmoratus has been given to the condition. Other cases of this type have been described by Anton[36] and Bielschowsky.[37] Twenty-three pathologically verified cases were reported up to 1936. Four cases of this sort were reported by Löwenberg and Malamud,[38] of which two were typical instances of diplegia. In one of these cases there was a small brain, with atrophy and microgyria. The striatum and thalamus had the typical appearance of status marmoratus. In the caudate nucleus, putamen and thalamus there was also severe gliosis with great destruction of ganglion cells. There were cell loss and gliosis in the cortex also. The condition varied from total destruction of all the layers to only slight involvement. The third cortical layer suffered more than the others. In a second case there were atrophy and microgyria. In addition, there were diffuse destruction of the cells of the cortex and the ganglion cells of the caudate nucleus, putamen and thalamus, accompanied by gliosis. In these areas there was the typical picture of status marmoratus. Sometimes, as in the case of Bielschowsky, status marmoratus has been observed in the cerebral cortex as well as in the striatum. Cases of status marmoratus are rare.

Status Marmoratus: Meyer and Cook[39] reported two cases in which status marmoratus was seen, respectively, in the striatum and in the thalamus. In both there had been mental deficiency and cerebral diplegia from infancy. The lesions were present not only in the neo-

35. Vogt, C., and Vogt, O.: Zur Lehre der Erkrankungen der striären Systems, J. f. Psychol. u. Neurol. **25**:660, 1920.

36. Anton, G.: Ueber die Beteiligung der grossen basaler Gehirnganglien, Jahrb. f. Psychiat. u. Neurol. **14**:141, 1896.

37. Bielschowsky, M.: Ueber den Status marmoratus des Striatums, und typische Markfasergeflechte der Hirnrinde, J. f. Psychol. u. Neurol. **31**:125, 1924.

38. Löwenberg, K., and Malamud, W.: Status Marmoratus; Etiology and Manner of Development, Arch. Neurol. & Psychiat. **29**:104 (Jan.) 1933.

39. Meyer, A., and Cook, L. C.: État marbré, J. Neurol. & Psychopath. **16**:341, 1936.

striatum but in the pallidum, substantia nigra, dentate nucleus, olivary bodies and cerebellum. For this reason Meyer and Cook concluded that it is erroneous to regard status marmoratus as a systemic disease of the striatum.

Paraplegia.—Spastic Type: Cases of paraplegia in which necropsy studies were made are not numerous. Ferguson [40] reported such a case. He observed a "patch of sclerosis at the upper end of each Rolandic fissure extending back on the ascending parietal convolution rather more than forward on the ascending frontal." There were distinct atrophy of the cortical cells in the affected areas and degeneration of the pyramidal tracts. Steinlechner [41] in his case noted bilateral porencephaly, accompanied by failure of development of the pyramidal tracts. A similar condition was seen in Ross' case.

On these few cases is based knowledge of the pathologic lesions in spastic paraplegia (diplegia group). They are not numerous enough for the establishment of any single lesion or group of lesions as the essential pathologic background of spastic paraplegia.

Atonic Type: Foerster [42] described four cases of what he called the atonic-astasic type of cerebral diplegia, characterized by atonia, mutism and mental deficiency. In two cases in which autopsy was done there was lobar sclerosis affecting the frontal lobe and paracentral gyrus on both sides. The cerebellum was intact. Moreover, there were spastic manifestations in both cases. Similar cases were reported by Clark,[43] but without autopsy studies. Clinical studies were made also by Batten and von Wyss [44] and by Hunt.[45] Hempelmann [46] reported two cases. In one of these necropsy showed that the cerebrum and cerebellum were smaller on one side. The defect was regarded as developmental.

REPORT OF CASES

Material for necropsy studies on cerebral diplegia is not easily obtained. Many of the patients die in institutions for the feebleminded, so that the central nervous system is not readily available for study.

40. Ferguson, J.: Infantile Spastic Paraplegia, Am. J. Obst. **24**:928, 1891.

41. Steinlechner, A.: Ueber den Bau des Rückenmarkes bei Microcephalen, Arch. f. Psychiat. **17**:649, 1886.

42. Foerster, O.: Die atonisch-astatische Typus der infantilen Cerebrallähmung, Deutsches Arch. f. klin. Med. **98**:216, 1909.

43. Clark, Pierce L.: Infantile Cerebro-Cerebellar Diplegia of Flaccid Atonic-Astasic Type, Am. J. Dis. Child. **5**:425 (June) 1913.

44. Batten, F. A., and von Wyss, W. H.: The Atonic Form of Cerebral Diplegia, Brit. J. Child. Dis. **12**:65, 1915.

45. Hunt, J. Ramsay: Diataxia Cerebralis Infantilis, Am. J. M. Sc. **155**:503, 1918.

46. Hempelmann, T. C.: Cerebro-Cerebellar Diplegia, Arch. Pediat. **39**:411, 1922.

Nevertheless, we have collected data in several good cases of cerebral diplegia, which form the basis of this study.

Our first case is an excellent example of cerebral agenesis associated with diplegia.

CASE 1.—*Microcephalia, diplegia and idiocy's fetal brain, with almost complete agenesis of cortical structures and rudimentary basilar structures; absence of pyramidal tracts.*

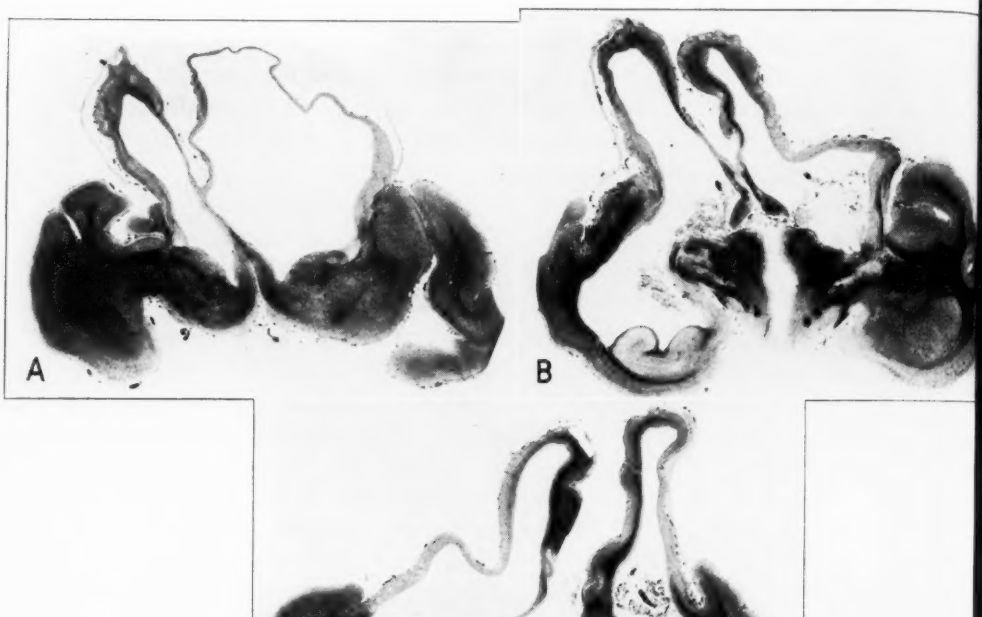

Fig. 1 (case 1).—Cerebral diplegia due to agenesis. Note the absence of cortex in all the sections, except for a rudimentary cortex in the supracallosal area (*B*) and in the temporal lobes. The striatum (*A*) is rudimentary and the rest of the base of the brain (*B* and *C*) is poorly developed. Weil stain.

History.—C. E., a white girl aged 2½ years, was admitted to the Philadelphia Institution for the Feebleminded on May 16, 1934. Her mother, father and three siblings were all living and in good health. The child was a twin; the other twin died of pneumonia at the age of 1 year. The patient's development was very slow, and she was never able to walk or talk. Her arms and legs were stiff, which left her completely helpless. She cried most of the time.

Clinical Examination.—The child was not much larger than an infant of 6 months. She weighed 12 pounds (5,443 Gm.). The head was microcephalic.

The eyes showed purulent nonspecific conjunctivitis. The pupils were normal and reacted to light. Despite this, she appeared to be blind. The nose was small, and the passages were encroached on by the high-arched palate. The chest and abdomen were normal. All four extremities were spastic and contracted, the lower extremities more markedly than the upper. The deep reflexes were hyperactive throughout, and there was a Babinski response bilaterally. The patient appeared to be sensitive to pin-pricks. Her mental age was 0.6 month, and her intelligence quotient was 0.02. The diagnosis was mental deficiency (low grade idiocy) associated with congenital cerebral spastic diplegia.

Gross Study of the Brain.—The brain was extremely small. The dura was firmly adherent to the cortex. The frontal, parietal and occipital lobes of each hemisphere were composed almost exclusively of a large porencephalic cyst. Only a few simple gyri were seen; the rest of the hemisphere consisted of a smooth fibrous cover. The temporal lobes were much better developed than the rest of the cerebrum. The brain on section showed a large porencephalic cyst in each hemisphere. These communicated with the ventricles. The cortex composing the roof of the cysts was abnomally thin, the corpus callosum was entirely absent, and the basal ganglions were much smaller than normal.

Histologic Studies.—The brain was poorly developed. It looked like the brain of a 7 month fetus, rather than that of a 2½ year old child. Studies of the myelin sheaths and cells revealed complete absence of the frontal, parietal and occipital lobes. Of the entire structure of the frontal lobe, only a rudimentary cingulate gyrus remained. The lobes were replaced by a thin membrane, under which was a greatly dilated lateral ventricle. There were no ganglion cells in the frontal, parietal or occipital lobes. The meninges were rudimentary and were composed of an outer layer of thick fibrous tissue containing a few vessels and of a thin inner layer with many vessels. The cells in the very thin structure which remained of the cortex were all astrocytes. There were no ganglion cells. Only the temporal lobes were present, and these too were greatly underdeveloped. Their gyri were poorly defined. Only the first temporal gyrus could be distinguished from the rest of the temporal lobe. The hippocampal gyrus was present in both temporal lobes, but it was poorly defined. The white matter in both temporal lobes took a good myelin stain, but there was little present. No myelin structure remained in the temporal cortex. Studies of the cells of the temporal cortex revealed indistinct lamination. The ganglion cells were infantile in type. They contained no Nissl substance, and their cytoplasm appeared vacuolated and fluffy. In the lamina pyramidalis (III) the number of ganglion cells was definitely decreased.

The basal ganglions were all poorly developed. The caudate nucleus and putamen were small, and their myelin structure was greatly decreased in amount. The striatal fibers were small and few. Nothing was seen which could be interpreted as pallidum except a small eminence in the striatal region. The entire thalamus was poorly developed and much smaller than normal. Its various nuclei could not be clearly seen. The nucleus ruber, on the other hand, was well developed bilaterally and stood out in contrast to the poorly demarcated nuclei elsewhere. The substantia nigra was not pigmented, nor could its cells be seen with the cell stains.

The pyramidal tracts could not be seen anywhere. There were no Betz cells in the cortex, no internal capsule, no cerebral peduncles, no pontile corticospinal tracts and no pyramids in the medulla. The lateral columns in the spinal cord

were smaller than normal, but no demyelination was present. In the pons, some of the corticopontocerebellar tracts could be made out in the upper third of the basis pontis. These were probably fibers from the temporal lobes. They were poorly myelinated. The inferior cerebellar peduncle was well developed, but the superior cerebellar peduncle was small and poorly myelinated and was indistinctly separated from the other structures of the brain stem. The mesial fillet was partially myelinated, but small. The posterior longitudinal bundle and hypo-

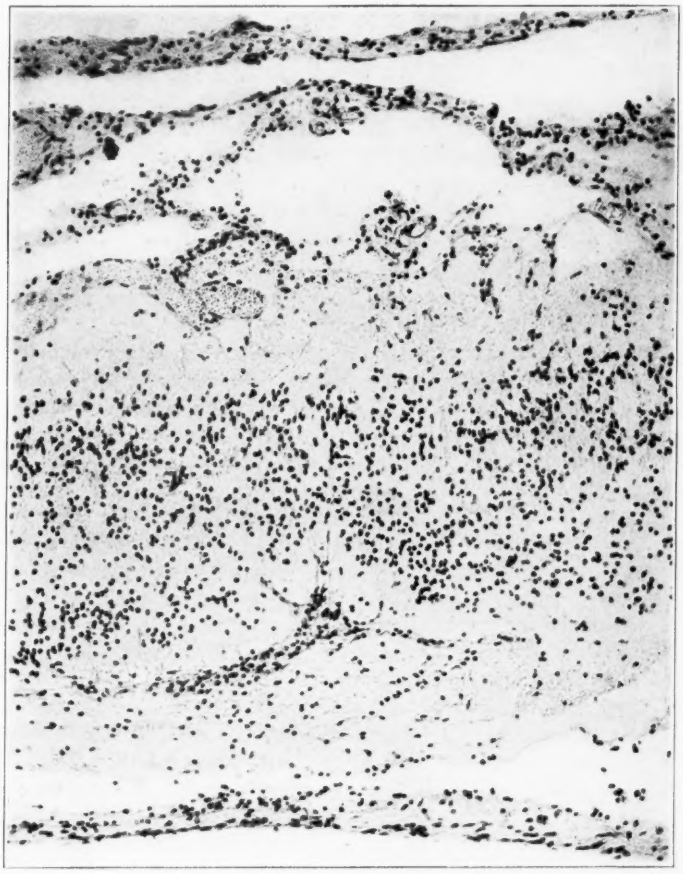

Fig. 2 (case 1).—A section through the entire width of the cortex. There is no lamination. Ganglion cells are not present. The cells are all neuroglial and are chiefly astrocytes. Hematoxylin and eosin stain.

thalamus were well developed. The spinal cord was very small but otherwise showed nothing abnormal. The anterior horn cells were normal in number, but smaller than usual. Their internal structure was not altered.

In this case, then, the brain was of fetal type, both in size and in development. It had no frontal, parietal or occipital lobes. Only the

temporal lobes were present, and these were poorly developed. There were no pyramidal tracts—only temporopontocerebellar tracts and a poorly developed neostriatum, thalamus and substantia nigra. There

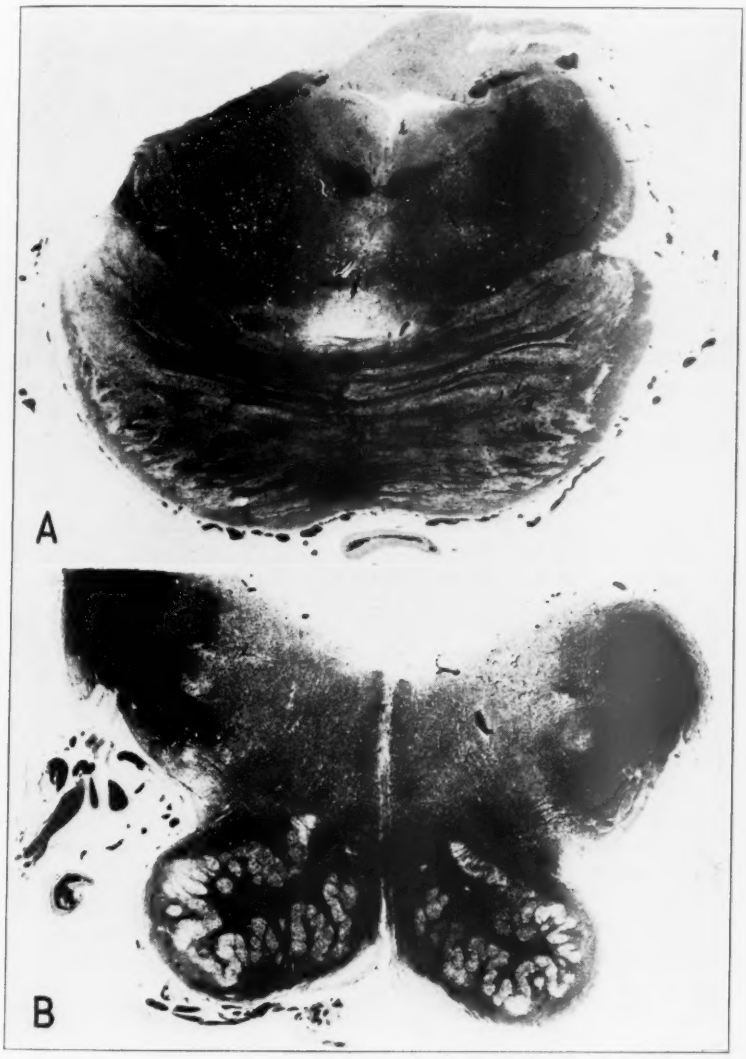

Fig. 3 (case 1).—In the pons (*A*) there are no corticospinal fibers and few corticocerebellar fibers. In the medulla (*B*) the pyramids are completely absent.

was no paleostriatum. In contrast, the nucleus ruber, the hypothalamus and the posterior longitudinal bundle were well developed.

The next case shows clearly that few abnormalities may be noted in the brain in a case of severe cerebral diplegia.

CASE 2.—*Typical cerebral diplegia without mental deficiency; mild degeneration in corticospinal system; more severe degeneration in neostriatum.*

History.—A. W., a white boy aged 13 years, was admitted to the Philadelphia General Hospital on Oct. 15, 1887, because of paralysis and inability to walk. He remained there until his death, at the age of 53. The condition had been present from birth. He was unable to lift his head normally, and his legs were always crossed. His mother died several years prior to his admission. His father died at the age of 30, of pthisis. The patient was the only child. He had had no other illness, no convulsions and no difficulties in sphincter control.

Clinical Examination.—The boy was underdeveloped, with only slight impairment of intelligence. The head was usually held to the right. There was marked spasticity of the entire musculature, and great effort was required to accomplish active or passive movements. The forearms were semiflexed, with the wrists extended. The metacarpophalangeal joints were flexed; the proximal interphalangeal joints were hyperextended, and the distal interphalangeal joints were slightly flexed. The thighs were adducted and crossed, and the legs were in extension. There was wasting of the lower extremities, more marked on the left. The deep reflexes were hyperactive, and there was bilateral ankle clonus. The abdominal reflexes were present, but the cremasteric reflexes were absent.

The mentality was surprisingly good. The patient showed little, if any, evidence of mental deterioration. He was unable to walk. Speech was dysarthric. In general the clinical picture was that of typical cerebral diplegia.

The pupils were equal and regular and responded normally. There seemed to be no involvement of the cranial nerves, but speech showed defective articulation.

Course.—On Dec. 5, 1900, the patient was operated on for a gangrenous undescended left testis. During May 1905 he had measles, and during June 1916, scabies. On April 18, 1927, he died of myocardial failure, which followed an attack of food poisoning.

Gross Examination of the Brain.—The brain was small, and weighed 1,150 Gm. There was generalized fibrosis of the pia-arachnoid, but otherwise little abnormality.

Histologic Studies.—The histologic changes were relatively few in proportion to the several clinical signs of cerebral diplegia. The cortex showed an adherent pia-arachnoid, which was moderately fibrotic. There was no disturbance of architecture or loss of cells in the agranular portion of the frontal cortex. In the precentral gyrus the Betz cells were normal in number, but showed definite changes. The nucleus was usually swollen, the nuclear outline indistinct, the Nissl substance lost and the cytoplasm swollen. This was true of almost all the Betz cells. The smaller ganglion cells in this gyrus were frayed, and the cytoplasm was vacuolated. The granular portion of the frontal cortex showed no loss of cells, but in the lamina granularis externa (II) and the lamina pyramidalis (III) the nuclei of the ganglion cells were swollen, pale and indistinct in outline, and the cytoplasm was completely frayed or shrunken. In some cases shadow cells were present.

The putamen and caudate nuclei showed great reduction in the number of the large ganglion cells. Those remaining were severely diseased and exhibited shrinkage of the cytoplasm, loss or pulverization of the Nissl substance and fat and lipoid. Neuronophagia was sometimes seen. The small cells also were severely diseased. There was only a moderate degree of gliosis. In the pallidum

the ganglion cells were more numerous than normal, owing probably to slight atrophy of this nucleus. There were no changes in the cells themselves.

The pyramidal tracts, despite the clinical evidence of diplegia, showed little abnormality. While the Betz cells were diseased, they were still present in normal numbers. Few signs of demyelination were observed within the corticospinal tracts. There were slight demyelination in the lateral column of one side in the cervical part of the spinal cord and slightly more marked demyelination in both the lateral and the anterior column bilaterally in the thoracic portion. The corticospinal bundles in the pons showed a mild degree of demyelination. Some of the corticocerebellar tracts were demyelinated, and the medial part of the cerebral peduncles was slightly demyelinated.

In this case the typical clinical picture of cerebral diplegia was shown. Histologic studies revealed only mild evidences of degeneration within the corticospinal systems—hardly enough to explain the severe diplegia. Degenerative changes were most marked within the neostriatum (caudate nucleus and putamen), which suggests that some of the rigidity might be of extrapyramidal origin. The cerebral cortex was well preserved for the most part.

In the following group of cases, the data are somewhat similar to those in case 2. The cases are characterized by the presence of lesions, chiefly in the extrapyramidal system.

CASE 3.—*Typical cerebral diplegia; loss of Betz cells in corticospinal system and of large neostriatal and pallidal cells in extrapyramidal system.*

History.—S. W., a Negro girl aged 6 years, was admitted on Aug. 5, 1930, to the children's ward of the Philadelphia General Hospital, to the service of Dr. W. M. Bradley. She had never walked or talked, nor had she ever been able to feed herself. Her parents were dead, and the informant, an uncle, did not know whether the child was born at term or whether instruments were used at the delivery. Four days before admission she became feverish; the next day she was drowsy and refused food. The day before admission she became unconscious.

Physical Examination.—The child was unconscious, with hot, dry skin. She lay on her back and held the forearms and fingers flexed, with occasional tremors of both hands. The pupils were small and fixed. Movements of the eyes could not be elicited. The breath had the odor of acetone, and the tongue was coated. There was no rigidity of the neck and no adenopathy. The ribs showed slight beading. The heart sounds were rapid and fairly strong. The right side of the chest did not move during respiration, and there was impairment to percussion anteriorly and posteriorly up to the second rib on this side. The breath sounds were diminished, and there were many inspiratory rales. The left lung showed many scattered rales posteriorly. The abdomen was scaphoid, and many hard masses were felt, but the liver and spleen were not palpable. The lower extremities were thin and atrophic, with shortening of both achilles tendons and some equinovarus of the right foot. Both legs were spastic. The arms were thin and spastic, with resistance to passive movements. The hands were in the obstetric position. The tendon reflexes were markedly exaggerated, but there was no Babinski or Brudzinski response.

Urinalysis gave normal results. The blood count revealed nothing abnormal. Examination of the spinal fluid showed normal pressure, no cells or globulin and a negative Wassermann reaction.

Gross Examination of the Brain.—The brain was very small and weighed 800 Gm. There was little to be seen in the cerebral hemispheres. Both cerebellar hemispheres were poorly developed, only a small part of each being present.

Histologic Studies.—There was diffuse cell loss in the lamina pyramidalis (III) of the frontal area of the cortex. A similar loss was observed in the temporal and parietal lobes. There were no changes in the meninges and no evidence of gliosis in the cortex. The precentral gyrus contained no Betz cells. There was marked loss of the large ganglion cells in the caudate nucleus and putamen. The remaining large cells were severely diseased; the nuclear outlines were indistinct, and the cytoplasm was vacuolated and showed loss of Nissl substance. A similar

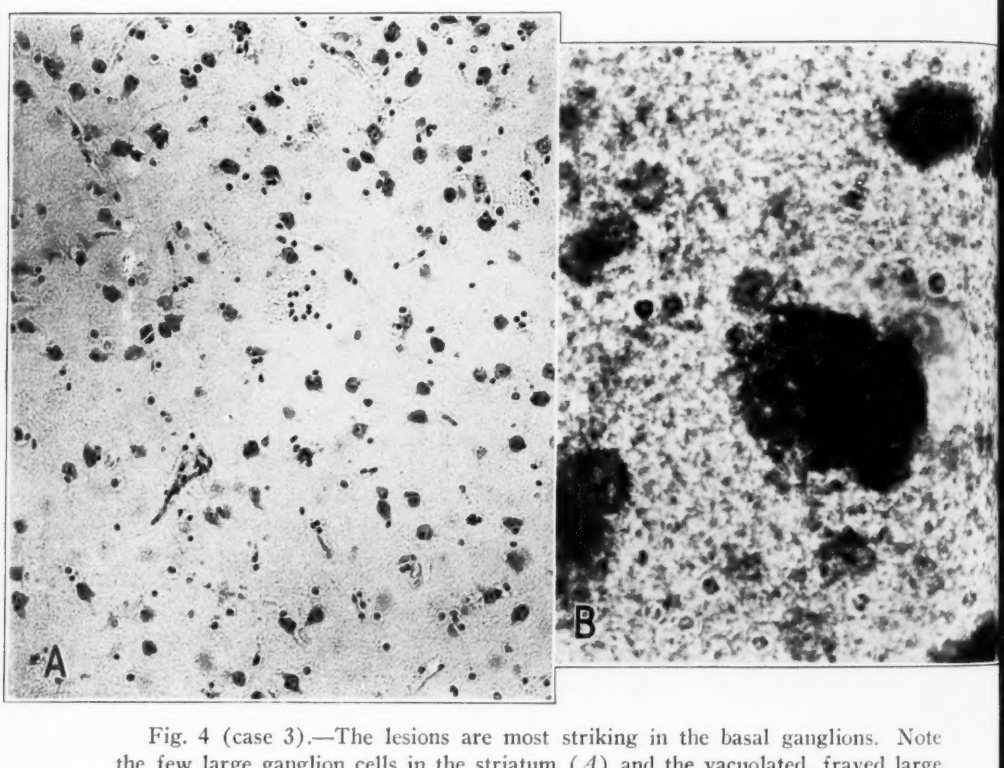

Fig. 4 (case 3).—The lesions are most striking in the basal ganglions. Note the few large ganglion cells in the striatum (*A*) and the vacuolated, frayed large ganglion cell *B*.

cell loss involved the large ganglion cells of the pallidum. The remaining cells showed changes similar to those in the putamen and the caudate nucleus. The cells of the thalamus showed nothing abnormal. The large and small ganglion cells of the nucleus ruber were in good condition. No changes were seen in the substantia nigra.

In this case there was typical cerebral diplegia, with loss of the Betz cells in the corticospinal system and loss and disease of the large neostriatal and pallidal cells in the extrapyramidal system.

CASE 4.—*Cerebral diplegia with mental deficiency; internal hydrocephalus; minor cortical changes; degeneration of large neostriatal and pallidal cells; intact corticospinal system.*

History.—S. H., a white girl, was admitted to the Philadelphia Institution for the Feebleminded on March 14, 1925, at the age of 5 years. Her mother, father and six siblings were all living and well. She had a normal birth, and teething, talking and walking developed normally. She was a bright child until she was taken ill with spinal meningitis, at the age of 1 year. After that she was irritable, refused food and became incontinent. She was unable to sit, stand, talk or feed herself.

Clinical Examination.—The child was fairly well nourished, but underdeveloped. Her head was large, with prominent frontal bosses. She passed an unusual amount of urine. There was internal strabismus. The pupils reacted normally to light. The muscles of the extremities were flabby, and the feet were cyanotic. The skin was rough and dry and showed vasomotor instability. She did not walk, sit up or raise her head. She refused to take nourishment. There was a moderate amount of spontaneous activity. On Dec. 27, 1925, her mental age was 3.6 months, and her intelligence quotient, 0.05. On Feb. 16, 1932, at the age of 12 years, her mental age was still 3.6 months. She was unable to sit, stand, talk or feed herself. She lay with thighs flexed and adducted and showed moderate spasticity of all extremities. The reflexes were hyperactive, but ankle jerks and the Babinski response were not elicited. The abdominal reflexes were present. She showed outbursts of temper, with occasional spells of crying and laughing.

Course.—She died suddenly on Jan. 2, 1934, at the age of 14. The diagnosis was chronic internal hydrocephalus with spastic diplegia.

Gross Examination of the Brain.—The brain was large and fluctuant. The gyri were swollen and edematous. There was severe internal hydrocephalus involving the lateral and third ventricles. The corpus callosum was much thinned, and the basal ganglions were compressed and flattened.

Histologic Studies.—The cerebral cortex showed abnormalities with the cell stains, but did not show them with the myelin sheath stains. There was no demyelination anywhere in the brain. The cells in the lamina pyramidalis (III) showed diffuse decrease in number. The Betz cells were normal in number and appearance. The large ganglion cells of the caudate nucleus and putamen were decreased in number. The remaining large cells were swollen and contained fat. The small ganglion cells in these nuclei were normal in number and appearance. The ganglion cells of the pallidum were likewise reduced in number. The remaining pallidal cells showed loss of Nissl substance, shrunken and distorted cytoplasm and a pyknotic nucleus. The nucleus ruber, substantia nigra, cerebellum, medulla, spinal cord and other parts of the brain and brain stem were normal.

CASE 5.—*Typical cerebral diplegia with mental deficiency; loss of cells in lamina pyramidalis; loss of Betz cells; mucocytic degeneration in white matter of cortex; severe disease of large cells of caudate nucleus and putamen.*

History.—A. C., was the third of three children. In the first pregnancy there was a placenta praevia, and birth occurred at 7 months. The infant died after one week. The second child was a girl, who was normal and is now married. The third child, the patient, was born five weeks prematurely and weighed only 6 pounds (2,722 Gm.) at birth. She seemed normal at birth, but collapsed on the ninth day of life, after which she was never normal. She became spastic

in all limbs at this time and remained so until her death at the age of 21 years. She had numerous athetoid movements. The head was usually pulled backward and to the right. The spasticity increased as the patient grew older. She was never able to talk. Both sight and hearing were normal. Her mentality was

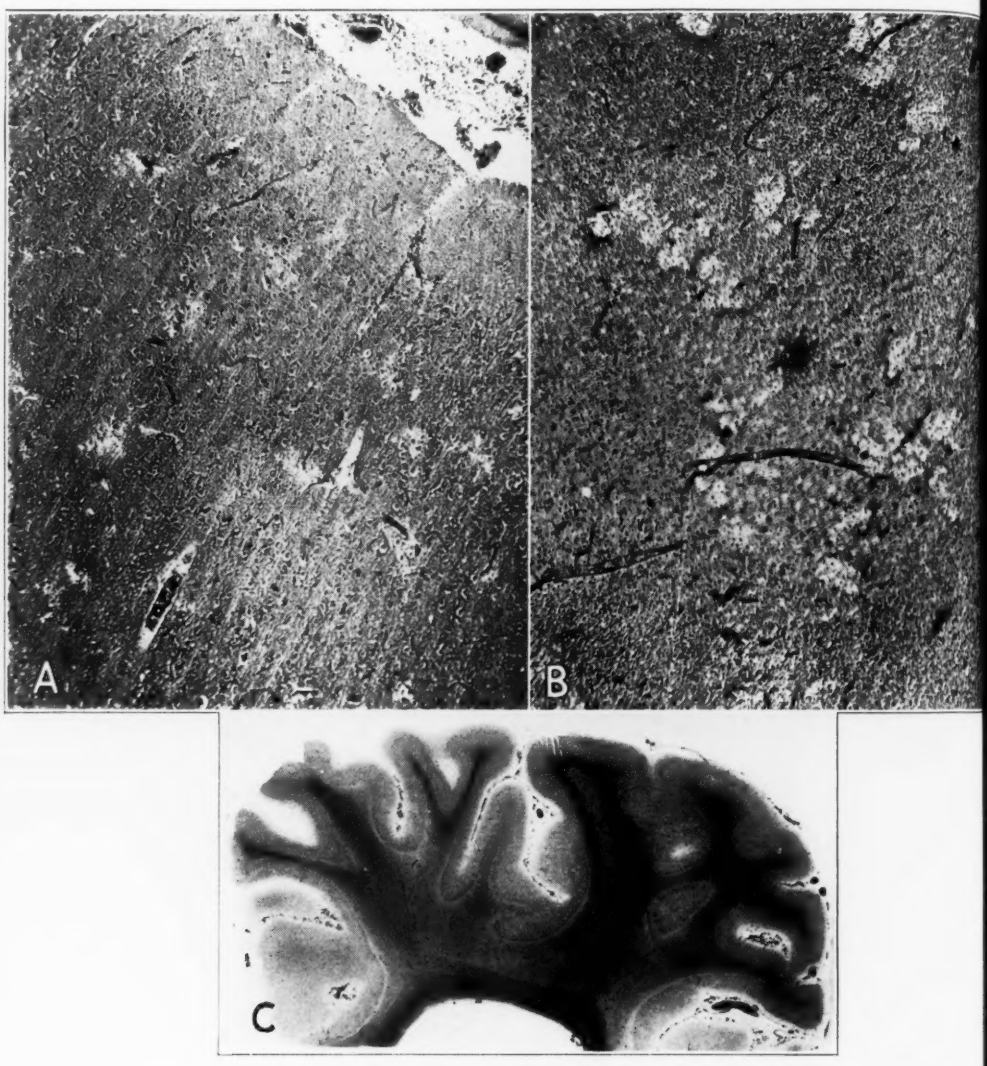

Fig. 5 (cases 5 and 7).—Mucocytic degeneration is seen (*A*) in the cortex and (*B*) in the white matter (case 5). Note how diffuse the process is. The myelin sheaths in the subjacent white matter (*C*) are greatly demyelinated (case 7).

subnormal, but she was by no means idiotic. Her mother estimated her mental level as that of an 8 or 9 year old child. She had definite spastic diplegia with athetoid movements.

Histologic Studies.—Over the cortex there was mild pial fibrosis. The cortical architecture was well preserved. There was patchy loss of cells in the frontal areas and, to a lesser degree, in the parietal and occipital areas. This loss was manifested as small cell erosions or as extensive laminar cell loss extending over a whole gyrus. The ganglion cells showed a variety of changes. In the frontal, parietal and temporal areas there was loss of Nissl substance, with vacuolation of the cytoplasm and swelling of the cells. There was marked edema of the cells of the lamina granularis externa (II) and of the upper portion of the lamina pyramidalis (III). The Betz cells of the motor cortex were greatly reduced in number. Only a few remained, and these showed the characteristics of axonal chromatolysis. The smaller ganglion cells in the motor area also showed such changes, but to a lesser degree. The white matter was filled with vacuoles and in some places contained areas of mucocytic degeneration.

The large cells of the caudate nucleus and putamen were greatly decreased in number. The remaining cells were diseased; they showed vacuolated cytoplasm, loss of Nissl substance and an increased amount of pigment. The small ganglion cells in these nuclei showed chronic cell changes—shrunken, dark cytoplasm and nucleus and tortuous cell processes. The pallidum showed slight decrease in the number of ganglion cells, but otherwise nothing abnormal. The thalamus, substantia nigra, nucleus ruber, pons and medulla showed nothing abnormal. There was surprisingly little degeneration in the corticospinal tracts, despite the disease of the Betz cells. There was a slight degree of demyelination of the pyramidal tracts in the lateral columns, but elsewhere the fibers of this tract were normal.

In this case of cerebral diplegia with mental deficiency, there were cell loss in the lamina pyramidalis (III) out of all proportion to the age of the patient, loss of Betz cells, mucocytic degeneration in the white matter of the cortex and severe disease of the large striatal cells. The changes in the brain account more or less adequately for the clinical picture. The spasticity, however, is not adequately explained by the corticospinal changes, for the degeneration in this tract was not marked and could hardly have accounted for the severe spasticity present during life.

CASE 6.—*Cerebral diplegia; minor changes in corticospinal system.*

History.—J. H., a white boy, was admitted to the Philadelphia Institute for the Feebleminded on April 11, 1925, at the age of 4 years. His parents and a brother were living and well. A paternal uncle was mentally deficient. The mother was critically ill with appendicitis before the birth of the child, and labor was induced. The child was born one month before term. Ether anesthesia and forceps were used. The child teethed at the age of 6 months, held up his head at 2 years and sat up at 2½ years. He never walked or talked. At the age of 18 months convulsions occurred; at 2 years he had pertussis; at 2½ years, measles and at 4 years, chickenpox. In the hospital he improved slowly, but he never was able to care for himself.

Clinical Examination.—Examination on Nov. 26, 1926, showed that he was underdeveloped and poorly nourished. He had a somewhat large head. The pupils and extra-ocular movements were normal. The teeth were poorly erupted, and the gums were inflamed. There was flexion contracture of all the extremities. The reflexes were hyperactive. There was apparently no paralysis. Mental

examination on March 11, 1930, when he was 9 years and 8 months old, showed a mental age of 4.8 months, with an intelligence quotient of 0.07. He was considered to be a low grade idiot, hopelessly untrainable, with congenital spastic diplegia and questionable hydrocephalus.

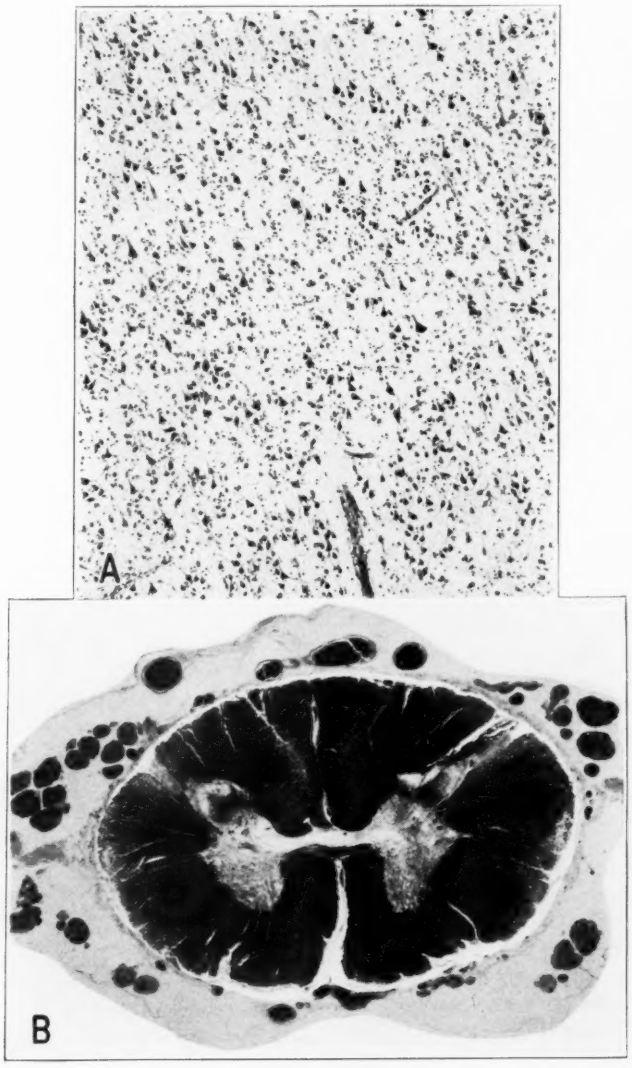

Fig. 6.—There were few lesions in the nervous system. In *A* (case 6), the precentral gyrus shows a normal number of large motor cells. In *B*, the spinal cord of a man aged 45, with cerebral diplegia since birth, there is only slight demyelination in the region of the spinocerebellar tracts and the fasciculus gracilis.

Gross Examination of Brain.—The brain was noticeably small for a child of 11. There were simplicity of pattern of the gyri and a slight degree of atrophy of the frontal gyri. A mild degree of internal hydrocephalus was present.

Histologic Studies.—In the cortex there were diffuse cell losses, particularly in the lamina pyramidalis (III) in the frontal areas. These were severe in some parts, so that few cortical cells remained either in this lamina or in other layers. The Betz cells were greatly reduced in number, and those which remained showed swelling of the nucleus and nucleolus, shrinkage and distortion of the cytoplasm and loss of Nissl substance. The ganglion cells in all parts of the cortex were palely stained and swollen. The large ganglion cells of the caudate nucleus and putamen were severely diseased, and most of them were gone. The remaining cells had frayed, broken cytoplasm. There was hyalinization of the small vessels of the striatum. The other basal ganglions were normal. The Purkinje cells showed nothing abnormal.

In this case, more than in any of the others, there was great discrepancy between the clinical findings and the pathologic background. The loss of Betz cells hardly accounts for all the spasticity, while the cortical changes were not sufficient to explain the idiocy.

CASE 7.—*Cerebral diplegia; diffuse areas of mucocytic degeneration in the cortex and white matter; demyelination of the white matter and cortex.*

History.—No history was available in the case of S. L. It is known only that he had cerebral diplegia.

Histologic Studies.—Throughout all layers and involving diffusely all parts of the cerebral cortex were foci of degeneration. These were present also in the white matter. They had a grapelike appearance. In such areas the ground substance was degenerated and destroyed, but there was no gitter cell formation. The ganglion cells in these areas had disappeared. Around them the glia cells were swolen, but there was no glial hyperplasia. The swelling involved both the oligodendroglia cells and the astrocytes, but chiefly the former. In the white matter most of the glia cells were swollen, particularly in the degenerated areas. The cytoplasm of the glia cells was greatly swollen and appeared homogeneous. In many the cell membrane had disappeared. Often there was spoke formation around the nucleus, without any cytoplasmic contents in the cell. There appeared to be mucin around the vessels. The oligodendroglia cells were not proliferated. These cells were chiefly involved, but sometimes the astrocytes were affected. The basal ganglions and the base of the brain were normal.

Myelin stains revealed loss of myelin under the cortex, which involved the arcuate fibers. The myelin in the internal capsule on one side was thinned. The fibers of the tapetum, close to the ventricular wall, were well preserved as compared with the fibers of the centrum ovale, which were demyelinated. The fibers at the edge of the spinal cord showed some demyelination, but there were no lesions in the pyramidal tracts.

In this case of cerebral diplegia there were diffuse areas of mucocytic degeneration in the cortex and the white matter, with extensive demyelination of the fibers of the white matter. The changes explain inadequately the clinical features. It is possible that the diplegia was the result of degeneration in the cortex, despite the fact that there were few changes in the corticospinal tracts.

SUMMARY OF PATHOLOGIC OBSERVATIONS

It is obvious from a mere recital of the cases of cerebral diplegia in which autopsy was performed as well as from a glance at the observations in our cases that many kinds of lesions are seen in this disease. As this apparently obvious fact has been frequently overlooked in a consideration of the pathogenesis and etiology of the disease, it should be emphasized. For purposes of clarity, we offer a classification of the pathologic conditions associated with cerebral diplegia. This we have compiled both from our own experience and from that of others. The following classification covers quite completely the various types of lesion associated with cerebral diplegia:

1. Cerebral agenesis.
2. Porencephaly.
3. Atrophic lobar sclerosis and diffuse cerebral sclerosis.
4. Status marmoratus.
5. Meningeal hemorrhage.
6. Relatively normal brain.

It may be desirable to consider these various types of lesion seriatim, in order to appraise their importance in the production of cerebral diplegia.

1. *Cerebral Agenesis.*—This accounts for not a few cases of cerebral diplegia. Its manifestations vary greatly. There may be, as in case 1, almost complete failure of development of all parts of the brain and brain stem. Or there may be sufficient maldevelopment of only parts of the brain to produce cerebral diplegia. This is seen when there is absence of the pyramidal tracts or a focal lesion involving the precentral areas. In these instances of cerebral agenesis the causative process is probably intra-uterine.

2. *Porencephaly.*—In many cases cerebral diplegia is associated with porencephalic cysts. These are almost always bilateral. Many cases of cerebral diplegia are probably lost in the literature on porencephaly. The cause is intra-uterine in some cases and extra-uterine in others. In cases of the latter porencephaly results from softening, trauma or an inflammatory lesion.

3. *Atrophic Lobar Sclerosis.*—Many cases of cerebral diplegia have been reported under this heading. This type of sclerosis consists simply of focal atrophy of the brain, with loss of ganglion cells and replacement by astrocytes. The loss may be moderate, affecting only some of the cell layers, or it may be so complete as to wipe out almost the entire ganglion cell population of the affected area. There is always demyelination of the cortex. The process is not confined to the cortex alone;

it affects the subjacent white matter as well, causing demyelination, atrophy or disintegration of the axis-cylinders and glial scar formation. The lobar sclerosis usually involves the two hemispheres unequally. It affects single gyri or lobes of one or both hemispheres. It must be regarded as a secondary process in the majority of cases. It may be the result of inflammation (Long-Landry), of trauma, of meningeal hemorrhage (MacNutt) or of vascular occlusion (Gowers, Norman). In some cases it is probably the result of intra-uterine disease, but in the majority of instances it is produced by extra-uterine causes or factors associated with the process of birth.

4. *Status Marmoratus.*—This condition has been well described (Vogt; Bielschowsky; Löwenberg and Malamud) and needs no formal description here. It accounts for a relatively few cases of cerebral diplegia, usually those in which there is athetosis. In most cases it must be regarded as having an intra-uterine cause, probably a congenital defect of some sort (Vogt), but in some instances it is probably the result of infection (Löwenberg and Malamud). It has been regarded by some authors as the result of birth trauma. It is difficult to know when status marmoratus is the cause of cerebral diplegia. The diagnosis is usually made post mortem, but it is safe to say that cerebral diplegia associated with idiocy and athetosis may be the result of status marmoratus. It is not possible to be more definite than this.

5. *Meningeal Hemorrhage.*—The role of meningeal hemorrhage is difficult to evaluate. There is no question that subarachnoid hemorrhage occurs frequently in brains of infants. Usually it is of no serious consequence and causes no symptoms. In some cases it is severe and forms a clot on the cortex which may produce atrophic lobar sclerosis by interference with the circulation of the brain beneath the clot. Eventually the clot becomes organized, and the result is severe adhesive meningeal fibrosis with atrophy of the underlying cortex. The evidence from MacNutt's necropsy material is not convincing. So-called atrophic lobar sclerosis was present, but the role of subarachnoid hemorrhage was proved only by inference and the results were not definite. Subarachnoid hemorrhage is probably not responsible for many cases of cerebral diplegia. Indeed, we should regard it as a rare cause of the condition.

Relatively Normal Brain.—Cases of diplegia in which the brain is relatively normal form an important group. In not a few well studied cases few lesions have been noted which could be regarded as responsible for diplegia. These cases have been referred to elsewhere and need not delay us here. There was nothing abnormal in a few instances; in others only minor changes in the corticospinal pathways were observed. How does one explain the cerebral diplegia in these cases? Infantile hemi-

plegias have been observed in some instances in which the pyramidal tracts were intact. Cases of this sort were studied particularly by Spielmeyer [47] and by Bielschowsky.[48] In Spielmeyer's case there was spastic left hemiplegia without a Babinski sign. This condition was present for two years before the death of the patient. Histologic study revealed a completely intact corticospinal system; the Betz cells were not damaged, but there was complete loss of the upper cell layers of the lamina pyramidalis (III) in the motor cortex. In Bielschowsky's two cases hemiplegia had existed for about twenty-one and sixteen years, respectively. In both instances the corticospinal systems were completely intact.

In such cases it is assumed (Spielmeyer) that the hemiplegia is due to isolation of the Betz cell layer from the other cortical layers. The hemiplegia is regarded therefore as the result of interruption of intracortical connections between the cells of origin of the corticospinal tract and the cells of the lamina pyramidalis (III). Where this interruption takes place is not clear, but it must be on the afferent side.

It is possible that this mechanism is also operative in the cases of cerebral diplegia in which there are few changes in the corticospinal system. It is unlikely, however, because the cell loss in the lamina pyramidalis is usually not so extensive as to lead to this type of paralysis.

Still another explanation is possible: At least some of the hypertonicity in cases of cerebral diplegia may be due to disease of the basal ganglions. This seems to be true in four of our cases, in which the changes in the neostriatum and the pallidum far exceeded those in the precentral gyrus. It is even possible that all the increased tonus in these cases it due to degeneration of the basal ganglions, especially in the pallidum, similar to that seen in some cases of parkinsonism or progressive pallidal degeneration. The not infrequent absence of a Babinski sign in the cerebral diplegias lends still further support to the theory that the extrapyramidal factor is the cause of the hypertonicity. It may be true therefore that in cases of cerebral diplegia associated with few or no changes in the corticospinal system the hypertonicity is due to extrapyramidal disease.

PATHOGENESIS OF CEREBRAL DIPLEGIA

A survey of the many pathologic lesions observed in cases of cerebral diplegia should soon convince one that a single cause of this condition is not possible. Efforts to assign a single cause are therefore

47. Spielmeyer, W.: Hemiplegia bei intakter Pyramidenbahn, Wien. klin. Wchnschr. **53**:1404, 1906.

48. Bielschowsky, M.: Ueber Hemiplegie bei intakter Pyramidenbahn, J. f. Psychol. u. Neurol. **22**:225, 1916-1918.

confusing. It is our belief that much more can be accomplished in the understanding of this disease by acceptance of a pluralistic causation than by insistence on a single cause common to all cases. The latter concept does not hold to the facts; the former, far from being purely a compromise, fits the facts much more readily.

The causes of cerebral diplegia may be intra-uterine or extra-uterine. The intra-uterine causes may be hemorrhage (Alpers and Patten [49]), infection (Alpers and Patten [50]) or developmental disorders of the germ plasm. Hemorrhages into the neuroblastic or germinal layer may result in destruction of a sufficient number of neuroblasts to prevent the proper development of the cortex (Alpers and Patten). Disease in the mother, whether toxemia or infection, may be transmitted to the fetus and may result in some form of cerebral agenesis (Alpers and Patten). The numerous cases of cerebral agenesis indicate clearly that intra-uterine causes are important in cerebral diplegia. Among the various intra-uterine factors which have been mentioned are alcoholism, syphilis and tuberculosis (Hutinel and Babonneix [51]). Collier [52] maintained that "arrest of development during fetal life not [due] to any event connected with birth is to be found in the brain in all those cases of diplegia in which the symptoms are present from the time of birth." For Collier " the essential anatomical cause of diplegia is a primary degeneration of the cerebral neurons." This seems to us to be too broad a concept of the disease. It is possible that in most cases cerebral diplegia is due to some intra-uterine cause, but this can hardly be true in every instance. Indeed, there are too many cases in which this is not true. Thus, porencephaly may result from trauma, hemorrhage or inflammation, all of which may occur at birth or shortly thereafter. Furthermore, atrophic lobar sclerosis may result from extra-uterine as well as from intra-uterine causes. In the majority of cases the cause is probably extra-uterine, but in some instances the condition may result from hemorrhage. While the role of meningeal hemorrhage has been greatly overrated, it must be conceded that atrophic lobar sclerosis may result from such a hemorrhage under the proper circumstances. Furthermore, vascular lesions, such as injury and thrombosis of the superior longitudinal sinus at the time of birth, are capable of producing the

49. Alpers, B. J., and Patten, C. A.: Cerebral Birth Conditions with Special Reference to the Factor of Hemorrhage, Am. J. Psychiat. **12**:751, 1933.

50. Alpers, B. J., and Patten, C. A.: Cerebral Birth Conditions: The Rôle of Intra-Uterine Infection and Intoxication in Man, Am. J. Dis. Child. **52**:144 (July) 1936.

51. Hutinel, V., and Babonneix, L.: La maladie de Little, Ann. de méd. et chir. inf. **15**:625, 1911.

52. Collier, J.: The Pathogenesis of Cerebral Diplegia, Brain **41**:1, 1924.

picture of atrophic lobar sclerosis (Gowers;[53] Norman). Birth trauma has been too highly regarded in the past as a possible cause of cerebral diplegia, but it is nevertheless true that severe trauma with cortical lacerations at birth is capable of causing a clinical picture somewhat akin to that of cerebral diplegia. However, we are not greatly concerned with the causes of cerebral diplegia but wish rather to indicate that in its causation both intra-uterine and extra-uterine factors are possible.

CONCLUSIONS

Many sorts of lesions associated with cerebral diplegia have been recorded.

A classification of the pathologic conditions accompanying cerebral diplegia is offered.

It is suggested that both intra-uterine and extra-uterine factors are responsible for cerebral diplegia, but that of these the intra-uterine causes are the more important.

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53. Gowers, W. R.: Clinical Lecture on Birth Palsies, Lancet **1**:709 (April 14) 1888.

STUTTERING

PROBLEM AND SUGGESTED TREATMENT

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Stuttering is a disturbance in the rhythm of speech, characterized either by an intermittent blocking or by a convulsive repetition of sound. Stuttering is of special interest to pediatricians, since it generally has its onset during early childhood and since it is practically the only problem of early childhood that, once established, tends to become more pronounced and to persist into adult life. Occasionally stuttering may develop in the adult, but as a rule this type of stuttering has not the same etiologic basis as the type generally observed. Stuttering which begins in adult life has either a purely hysterical or a definitely organic basis.

In spite of the fact that stuttering has been known from time immemorial, only a few concrete facts about the subject have been definitely established. The outstanding fact is that it occurs more commonly among boys than among girls; the proportion usually given is approximately 4 to 1. Secondly, once the stuttering is established it tends to become more pronounced and more firmly fixed. Oddly enough, this occurs during those years when the child's articulation as a whole tends to improve and to become more distinct.

Various attempts have been made to explain why stuttering is more common among boys. The majority of investigators have explained stuttering on a psychologic basis, as due to environmental influences during childhood. It has been pointed out that the competitive element is stronger among boys, that the boy offers more resistance to external authority and that his attachment to his mother tends to promote neurotic tendencies.

If the psychologic explanation is accepted, that stuttering is more common in boys than in girls because neurotic tendencies are more

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prominent in boys, how can this be reconciled with the finding that neurosis in later life is more common in the female, especially when it is realized that neurosis in general has its origin in the experiences of early childhood?

This preponderance of male stutterers has been explained on an organic basis. Because the circumference of the head of a boy is larger than that of a girl it has been claimed that stuttering may be due to cephalic pressure during birth, which is more likely to occur when an infant has a large head. We [1] have pointed out that myelinization occurs earlier in the female than in the male; it is possible that this may account for the more advanced linguistic development in girls and the greater tendency of boys to have defective speech.

All investigators have agreed that stuttering has its onset in childhood, but there has been disagreement as to the period in which the majority of cases of stuttering begin. West [2] investigated 10,268 school children ranging from the first grade to the twelfth (6 to 14 years). Several interesting conclusions were drawn by him. In the majority of the cases stuttering began after the age of 6. The great preponderance of male stutterers was caused by a rapid increase in their numbers between the sixth and the twelfth year. He found a marked drop in the number of stutterers in the pubescent period.

Boome and Richardson [3] examined 477 stuttering children. They described three age periods in which stuttering is most likely to begin or to become intensified if it is already established. The first period is at the age of 2 years, when the child begins to talk; the second period is between the ages of 5 and 6 years, at the beginning of school life; the third period is at about the age of 7 years, the period of second dentition. It is interesting to note, however, that of the 477 children, 337, or 71 per cent, began to stutter between the ages of 2 and 6 years and a greater number of children (94) started to stutter at the age of 2 years than at any other age.

Seth and Guthrie [4] claimed that the two crucial ages for the onset of stuttering are from 4 to 5 years and from 7 to 8 years. In our speech clinic at the Brooklyn Jewish Hospital the children in the stuttering group range from 2 to 12 years of age; 73 per cent of these children,

1. Karlin, I. W., and Kennedy, L.: Delay in the Development of Speech, Am. J. Dis. Child. **51**:1138 (May) 1936.

2. West, R.: The Phenomenology of Stuttering, Proc. Am. Soc. Study Disorders Speech, 1930, p. 1.

3. Boome, E. J., and Richardson, M. A.: The Nature and Treatment of Stuttering, New York, E. P. Dutton & Co., Inc., 1932.

4. Seth, G., and Guthrie, D.: Speech in Childhood, London, Oxford University Press, 1935.

according to the histories obtained from the mothers, began to stutter between the ages of 2 and 5 years.

Blanton and Blanton [5] stated the belief that in virtually every case stuttering begins with the beginning of speech, or certainly in early childhood.

The symptoms of stuttering in its more obvious forms are well known and have been caricatured in play and in song. In its earliest stages, however, it may manifest itself only as a slight hesitation in the child's speech. Another early expression of stuttering occurs in the following manner: A child while speaking suddenly stops as if groping for a word to express his thoughts. The parents, thinking this the effect of a limited vocabulary or of the superiority of the child's ideation to his proficiency in articulation, frequently supply the needed word. If one observes the child in such a situation one can usually notice an expression of gratification on his face as the word is supplied. This inconspicuous form of stuttering may go on for several months before the more severe symptoms present themselves. In the majority of cases the more noticeable characteristics of stuttering appear in the very beginning. The symptoms vary not only with different cases but with different situations in the same case. The most obvious features are the spasmodic contractions of the muscles concerned with speech, such as those of the lips, tongue, jaw and larynx. The spasm may be tonic, the parts involved remaining tense or showing only a slight quiver until the sound is forced through. In other cases the spasm is clonic, producing explosive repetition of the same sound. Often there is a tendency for the stuttering to be more pronounced on the consonants, particularly on velars and labials, such as p, b, m, k, and g.

Those with a more severe type of stuttering may manifest in addition muscular tension and spasmodic movements in other parts of the body. Some children while stuttering may jerk their heads backward; others may clench their fists and stiffen their entire bodies. We had a child at the Brooklyn Jewish Hospital whose mother said that "he talked with his feet," for the child would stamp his feet while stuttering. Because of parental punishment he stopped "talking with his feet," but when seen in the clinic he "talked with his hands." His entire body would stiffen; he would assume a lordotic position, with tightly clenched fists; he would throw his hands forward and his head backward, giving the momentary impression of undergoing a convulsive seizure.

The less evident symptoms of stuttering are the respiratory anomalies. In normal speech the thoracic and the abdominal phase of breathing are synchronized, inspiration being somewhat deepened and expiration

5. Blanton, S., and Blanton, M. G.: For Stutterers, New York, D. Appleton-Century Company, Inc., 1936.

prolonged. Normally, speech can be produced only during expiration. In stuttering the synchronous activity of the thoracic and of the abdominal muscles is likely to be disrupted. Muscular spasms may involve the thoracic muscles, the abdominal muscles or the diaphragm, separately or in one combination or another. During these spasms the stutterer frequently tries to speak on inspiration. He often aggravates his condition by making strenuous inspiratory efforts with the head thrown back and with the muscles of the neck and of the chest tense, gasping for breath until, apparently exhausted, he forces out the word on expiration.

In recent years some laboratory work has been done with stutterers. The most recent work is that of Kopp,[6] who did biochemical studies on stutterers and on nonstutterers. He found that stutterers have a higher level of serum calcium and of inorganic phosphorus than the nonstutterers and that the levels of potasium, total protein, albumin and globulin are lower in stutterers. Stutterers also have a higher level of blood sugar. However, all the figures quoted by this investigator fall within normal limits.

We come now to the emotional factors of stuttering. Today more than ever before, stress is being laid on the importance of the emotional patterns that govern everyday life. It is well recognized that any type of abnormality will cause the emergence of certain compensatory mechanisms, which will color, to a greater or lesser extent, the daily activities of an otherwise normal person. The stutterer, because of his defect, has naturally acquired certain emotional trends and characteristics. These tendencies and characteristics have been exaggerated and sentimentalized in the literature on the subject. One reads that the stutterer comes to look on his difficulty as a terrible affliction, that he tends to become seclusive, unfriendly and neurotic and that he has great difficulty in adjusting himself. According to Adler's theory of organ inferiority, the stutterer is impelled to overcompensate for his difficulty to such an extent that all his actions and attitudes are conditioned by his defective speech. Stutterers are often regarded as presenting certain innate emotional tendencies. Greene[7] even attempted to describe a stuttering type of personality, "whose family pattern might just as well be that of a juvenile delinquent, neurasthenic, or psychotic."

What are these emotional characteristics which the stutterer presents? Most of the observations of the emotional life of the stutterer have been made on the adult stutterer who has carried his difficulty with him since

6. Kopp, G. A.: Metabolic Studies of Stutterers, Speech Monographs **1**:117, 1934.

7. Greene, J. S.: The Stutter-Type Personality and Stuttering, New York State J. Med. **36**:757, 1936.

early childhood. He represents, more or less, the end result of various emotional adjustments to a difficulty which has great social implications. Naturally, stutterers have many characteristics in common, particularly in their reactions to speech situations. Many acquire a fear of speaking, a tendency to shyness, a sense of inferiority, a preference for small groups, the habit of blushing and of palpitation before speaking and a tendency to use various devices to disguise the difficulty. The stutterer may become dominated by the idea of difficulty in speech. During conversation he knows beforehand the word on which he is going to stutter; he sees it clearly in his mind and frequently uses substitutions. The apprehension of stuttering may become so dominant that the stutterer who has no difficulty in certain situations begins to stutter in those same situations if he happens to ask himself why he does not stutter. Eventually he may indulge in self-pity and may use his speech difficulty to rationalize all his shortcomings and failures.

The stutterer's personality as a whole, however, is just as varied as that of the nonstutterer, and if one allows for his attitudes toward speech, his emotional characteristics are as normal and as varied as those of the nonstutterer. He certainly is not handicapped in his adjustment to everyday life. Stutterers are found among physicians, dentists, lawyers, clerks, musicians, preachers, laborers, kings and statesmen. As for the spiritual bond that is supposed to exist among stutterers, it is a fact that stutterers do not prefer to associate with one another.

Investigation of the emotional background of the stuttering child does not reveal outstanding behavior problems different in degree or in kind from those of the nonstutterer. The individual problems of such a child will depend greatly on his environment. There is, however, a difference in the emotional response to stuttering between the preschool child and the school child. The child who begins to stutter with the beginning of speech, or the preschool child who apparently talks well for a while and then begins to stutter, is confronted by the reaction of his parents, particularly that of his mother. His attention is drawn to his speech, and often punitive measures are undertaken as a means of correction. The child, whose emotional life at this period depends almost exclusively on his immediate home environment, becomes speech conscious. He may resent the corrections or the disciplinary measures and may become irritable and resentful. Even in homes in which there is a tendency to ignore the child's speech there may be emotional problems in the group surrounding the child which promote in him a feeling of insecurity and emotional instability, with the result that the stuttering becomes more pronounced and more definitely fixed.

These children, however, present as great individual variations as the nonstuttering children. Many of them, except for their stuttering,

present no behavior problems, real or implied, no matter how much one would like to find such problems.

As the child grows older his stuttering becomes more firmly fixed, and on entering school he has to make new adjustments. Gradually his reactions to the speech difficulty begin to show some of the traits one observes in the adult. He refrains from asking questions in the classroom; he begins to know that he is going to have difficulty with certain sounds and words, and he resorts to substitutions and other aids to speech. He becomes sensitive to ridicule and acquires some fear reactions which may result in blushing and in palpitation before speaking.

There has been investigation on the relation between stuttering and progress in school. It has been found that the intelligence quotient of the stutterer is within the same normal range as that of the nonstutterer. Wallin [8] in his survey of speech defects in St. Louis in 1915 and 1916 found that stutterers were retarded one and six-tenths years. We did not make any special study of this problem, but from our general observation of the patients in the clinic we found that, all other factors being equal, the educational progress of the stutterer was normal. However, in the oral English class, where his mark and progress depended on his speaking ability, the stuttering child often compared unfavorably with other children.

Outside of the immediate speech situation, however, the child at this period of life has so many absorbing interests and activities beyond the sphere of home and school that he as a rule reacts to his difficulty with more or less indifference. One may call this a latent period in the emotional influence of stuttering on his personality. He does not feel himself greatly handicapped. All the stuttering children we observed were active in the sports and the play of their own age groups. Our observations coincide with those of Johnson,[9] who made a careful study on 80 stutterers whose ages ranged from 7 to 42 years. He concluded that stutterers as a group have relatively normal emotional and social adjustment. He stated that in childhood, especially, the difference in adjustment between stutterers and normal nonstutterers was shown to be insignificant.

One finds abnormal attitudes or problems arising from the stutterer's associations, either at home or in the school. We interviewed a mother who had read something about the relation of stuttering to handedness. She proceeded to force her 7 year old boy, who was a stutterer and was right handed, to change to left handedness. She spent several hours daily playing ball and tennis with him, insisting that he

8. Wallin, J. E. W., cited by Fletcher.[11]

9. Johnson, W.: The Influence of Stuttering on the Personality, University of Iowa Studies in Child Welfare, Iowa City, University of Iowa, 1932, vol. 5, no. 5.

give preference to his left hand. The boy became irritable and unhappy, and his stuttering became more pronounced. Likewise, a teacher who has some pet theories about the treatment of stuttering may succeed only in aggravating the child's defect.

As to the cause of stuttering, the indications at present are that it is functional and not organic. Careful physical and special neurologic examinations do not reveal any defects of the organs of speech or of the nervous system. There are many theories about stuttering which help one to understand the problem. But the multiplicity of these theories disproves the adequacy of any one of them, and some of them display the arrant dogmatism which is characteristic of the literature on this subject. The emotional background of stuttering is recognized in all the modern theories, but it is of interest to note that even those men who approach stuttering from a purely psychologic point of view feel the need to define the difficulty more accurately in organic terms. Blanton,[5] who is well known for his psychiatric approach to stuttering, while he concluded that stuttering is essentially a difficulty of personality, stated the belief that the physical symptoms of stuttering are caused by an emotion that blocks off the control of the cortex over the thalamus and over the lower nerve centers. Brown,[10] who approached stuttering from the point of view of mental hygiene, declared it to be a disorder both of personality and of behavior. He amplified his theory with the statement that stuttering is the result of a temporary interference of the lower centers with cerebral control of the speech mechanism, such interference being caused by the emotion-producing content of the situation in which speech is required. Fletcher[11] described stuttering as a form of social maladjustment.

Bluemel[12] had a theory that stuttering results from transient auditory amnesia—the stutterer can not clearly hear in his mind the difficult word. Later he modified his theory. Adopting Pavlov's work, Bluemel came to regard speech as a conditioned reflex and stuttering as partial or intermittent inhibition. The young child is susceptible to disturbance in speech because his conditioned reflex of speech is immature and not yet firmly fixed. This immaturity renders him liable to inhibition as a result of shock or illness. Swift[13] stated a theory that stuttering is due to loss or diminution of the power of visualization. A stutterer has

10. Brown, F. W.: Personality Integration as the Essential Factor in the Permanent Cure of Stuttering, Ment. Hyg. **17**:266, 1933.

11. Fletcher, J. M.: The Problem of Stuttering, New York, Longmans, Green & Company, 1928.

12. Bluemel, C. S.: Stammering and Allied Disorders, New York, The Macmillan Company, 1935.

13. Swift, W. B.: Visualization Is the Best Method for Stammering, Proc. Am. Soc. Study Disorders Speech, 1930, p. 83.

partial or complete loss of visual imagery of the object for which the word stands. Swift declared that the anatomic basis of this disturbance is in the cuneus.

Greene [7] discussed a stuttering type of personality that comes of neuropathic stock and demonstrates neuropathic tendencies. Adopting Seemann's [14] conclusions on stutterers, Greene [7] stated that stuttering is caused by instability in the functioning of the vegetative nervous system. The "stutter type" person shows dominance of the parasympathetic system and he experiences a continued conflict between parasympathetic and sympathetic characteristics. In all probability this is due to the fact that he is a cross between the sympathetic type of the father and the parasympathetic type of the mother, or vice versa; thus a combination of the two has been created, with each system striving for dominance.

The psychoanalytic school, of course, regards stuttering as a pure neurosis. Coriat [15] referred to stuttering as an oral neurosis in which the libido becomes fixed at the oral erotic stage of development. Fenichel [16] stated that stuttering is an organ neurosis. Under the heading of pregenital conversion neurosis he discussed three entities: stuttering, bronchial asthma and psychogenic tic.

One theory that stresses the organic basis for stuttering is Travis' [17] theory of cerebral dominance. According to Travis, stuttering is mainly the result of a conflict between the two cerebral hemispheres which is caused by the lack of development of a dominant gradient. Stuttering is related to left handedness, in that normally left-handed children who are forced to use their right hand may acquire a stutter because of lack of development of the dominant hemisphere.

Our conception of stuttering, which developed in the light of present day knowledge, is that stuttering is the result of a neuromuscular incoordination, psychogenic in origin. Speech has a complicated mechanism. It requires a fine coordination of various muscle groups whose original function was not to produce speech but rather to fill the more primary needs of life. No doubt there is some structural weakness in this mechanism which predisposes a person to stuttering. In the early stages of stuttering, environmental factors play a dominant role in its establishment and fixation. Later on, the stutterer may acquire certain characteristic emotional traits which are especially pronounced in situations

14. Seemann, M.: Ueber somatische Befunde bei Stotterern, Monatschr. f. Ohrenh. **68**:895, 1934.

15. Coriat, I. H.: Stammering, a Psychoanalytic Interpretation, Washington, D. C., Nervous and Mental Disease Publishing Company, 1928.

16. Fenichel, O.: Outline of Clinical Psychoanalysis, Albany, The Psychoanalytic Quarterly Press, 1934.

17. Travis, L. E.: Speech Pathology, New York, D. Appleton-Century Company, Inc., 1931.

involving speech. On the whole, however, stutterers make a good adjustment to life, and many of them, by themselves, make an adequate adjustment to their difficulty of speech. If stuttering must be classified, it should probably come under the heading of neurotic traits. At present, certainly, no organic basis for stuttering is known.

As to prognosis, "once a stutterer, always a stutterer" has been the opinion of some well known authorities in this field, while others have claimed that a cure is possible for all. The laity as well as many physicians rely freely on the belief that "the child will outgrow it." Milisen and Johnson [18] in a study of approximately 8,000 public school children stated that of the total number of stutterers 42 per cent outgrew the disorder without clinical assistance. In our speech clinic at the Brooklyn Jewish Hospital, 50 per cent of the preschool stutterers (between 2½ and 5 years of age) ceased to stutter with minimal therapy after visiting the clinic only two or three times. However, no one can possibly predict which child will recover from his stuttering, and for this reason proper treatment is advisable in every case.

The treatment of stuttering must be both medical and educational. It must be medical because the doctor by his training is enabled to view the total personality of the child both from the physical and from the mental aspect. He gains insight into the personal life of the child and into the environmental factors surrounding him. Using these studies, he makes an effort to provide for the child the optimal conditions of health and of emotional stability. Treatment must be educational because the trained teacher of speech can help to observe and to analyze the various forms and shades of articulatory disturbance that the stutterer may present. The specialist in speech will then endeavor to understand the child's interests, to improve his attitude toward speech and to provide him with a good speech pattern. It goes without saying that (as in all difficulties dominated by emotional factors) it is the personality of the one who treats the condition, as well as the training itself, that determines the effectiveness of the treatment.

Treatment should begin as soon as stuttering is noticed. The best results are obtained with a preschool child between the ages of 3 and 5 years. The results in these cases depend greatly on the full cooperation of the parents. The treatment of the older school child is more difficult because he lacks motivation other than that given by his parents. Most of the time he is anxious to get the periods of treatment over as quickly as possible so that he may get back to his friends and to play. In the case of the adult, treatment should be more effective, because the adult seeks clinical help of his own free will and usually has an interest and a motive, vocational or social, for correcting his speech. The results to

18. Milisen, R., and Johnson, W.: A Comparative Study of Stutterers, Arch. Speech **1**:61, 1936.

be expected in the adult, however, should be spoken of in terms of improvement and control of speech, rather than in terms of a cure or complete freedom from stuttering.

The treatment given to a preschool child should be different from that given to a school child. In the Speech Clinic of the Brooklyn Jewish Hospital we use what we call the indirect approach with the preschool child. An investigation is made of the home surroundings and of the behavior problems of the child. The parents' attitudes and methods of correction are investigated. The family is assured that there is no organic basis for this difficulty. The child should be given a sense of security in the home without being pampered. Any arguments or controversial topics are to be avoided in the child's presence. The parents, especially the mother, should always take plenty of time in listening to the child and should never give him the feeling that he must hurry with what he has to say. The child should be allowed to use the hand he prefers. If he shows no definite preference, training in the use of the right hand should be undertaken, but without undue force and stress. All members of the family must avoid correcting the child's speech and must not manifest annoyance or anxiety in facial expression when the child stutters. The parents when talking to the child should use slow and distinct speech, in this way providing him with a pattern which he is capable of following.

The teacher of speech uses the play technic in winning the child's friendship and cooperation. She demonstrates a good speech pattern not only to the child but to the parents. She reads stories and rimes to the child and has him repeat them. She stimulates his interest and provokes spontaneous conversation and questions, striving constantly for good speech.

With the school child we use the more direct approach. The child's attention is drawn to the importance of good speech. Situations in both home and school, as well as the child's attitude toward his speech difficulty, are investigated, and an adjustment is attempted. It should be made clear to him that results will depend on his own will and on his interest in good speech. Relaxation and breathing exercises are used to minimize all tensions during speech. The individual problems of the child and their adjustments are discussed privately with him and then with the parents. The teacher of speech meets the children in small groups. No formal exercises in articulation are used, but from the beginning of treatment the exercises are in the form of good speaking.

In the treatment of an adult, the same method, in general, is used as in the treatment of the school child. With the adult, however, the discussion of the various problems is on a more mature level. No cure should be promised to the stutterer. He should be given an insight into the problem of stuttering so that he will form an objective attitude

toward his defect. This objective attitude will remove much of the feeling of fear and guilt that developed in relation to his stuttering. We believe, however, that the adult stutterer will speak with a minimum of difficulty, not only because of emotional adjustment but because of adhering to a pattern of speech which he is capable of following.

In the following outline we present the method used for the treatment of stuttering in the speech clinic of the pediatric department at the Brooklyn Jewish Hospital:

I. Complete physical and neurologic examination

II. Mental test to determine child's intelligence quotient

III. Interview with parents with special emphasis on:

A. Developmental history of the child

1. Type of delivery
2. Onset of teething
3. Onset of sitting
4. Onset of walking
5. Onset of talking
6. Muscular control; coordination
7. Handedness

B. Environmental history

1. Social and educational history of family
2. Temperamental history of family
3. Number of siblings
4. Parent-child relation
5. Child-sibling relation
6. Type of discipline in the home
7. Sleeping arrangements

C. Personal history of child

1. Chronological age and educational progress
2. Illnesses; mother's attitude and handling
3. Habits or neurotic traits, such as bed wetting, thumb sucking and masturbation
4. Temperamental and emotional attitudes such as timidity, aggression, self-reliance, friendliness, irritability, affection, coldness and a feeling of security

D. Speech history

1. Speech history of family
2. Language spoken at home
3. Onset of patient's speech
4. Type of early speech
5. Onset of stuttering; age
6. Cause of stuttering as given by parent
7. Type and degree of stuttering

8. Situations in which stuttering is most pronounced, lessened or absent
9. Any prolonged remissions from stuttering and the apparent cause
10. Parent's attitude toward the defect
11. Child's attitude toward his defect
12. Social reactions of schoolmates and playmates
13. Method of correction attempted by family or by other agents
14. Child's reaction to corrective methods
15. Devices child may use to help himself
16. Overt emotional reactions accompanying the disorder, such as blushing and tics
17. Other defects of speech

IV. Interview with child

A. To establish rapport

B. To pave the way for further contact

C. To analyze speech of child

D. To gain information about:

1. Earliest recollections
2. Play life
3. Fears and emotional conflicts
4. Attitude toward family, companions and school
5. Attitude toward speech difficulty and toward corrective measures
6. Interests and ambitions

V. Division of mentally normal children into the following groups:

A. Children aged 6 to 12 years

B. Preschool children

VI. Program of activities for the school child (group A)

A. Direct approach: child's attention directed to the importance of good speech

B. Individual conferences

1. Child seen individually from time to time and the various factors (IV, D) gone into in greater detail in an effort to better understand child's attitude and problems
2. Child given to understand that the reason for these discussions is the desire to help him
3. Special emphasis placed on the emotional problems that may be present at home, in school or outside
4. Child given an insight and understanding of his problems, and a cooperative attempt made to solve them or resolve them
5. Attempt made to develop in child a feeling of security and self-confidence
6. Technic of relaxation given
7. Suggestive treatment applied

C. Group activities and procedures

1. Progressive relaxation

(*a*) Purposes

(1) To lessen bodily tension

(2) To induce control of body and of emotions

(*b*) Activities

(1) Tensing of muscles later to be relaxed

(2) Relaxing progressively, beginning with the largest group of muscles and proceeding to the smallest

(3) Relaxation of whole muscular arc

2. Breath control

(*a*) Purposes

(1) To induce low, controlled, easy breathing

(2) To lessen tension in neck and shoulders

(3) To develop a more adequate breath span, with emphasis on controlled exhalation

(4) To coordinate breathing and phrasing

(*b*) Procedures

(1) Discussion of relation between exhalation and inhalation in speech

(2) Demonstration of "abdominal breathing"

(*c*) Activities

(1) Group exercise in controlled breathing

(2) Slow counting on controlled expiration

(3) Increasing the breath span; counting from 1 to 5 and from 1 to 10, progressively, for each exhalation

(4) Good duration pattern, giving full value to vowels instead of shortening them [19]

(5) Rhythmic phrases and sentences to be repeated for smoothness of phrasing with more frequent breath groups without damaging the inherent rhythm [19]

3. Reading

(*a*) Purpose: synthesis of objectives mentioned

(*b*) Procedure: group imitation of good pattern of speech, followed by individual presentation of it, through medium of rhythmic poetry and prose

(*c*) Activities

(1) Good speech pattern given by teacher through the medium of rhythmic poetry and prose

(2) Stutterer reads the selection with the teacher, then with the group

(3) Stutterer reads individually

(4) Stutterer again listens to good speech pattern

(5) Stutterer attempts to follow it alone

19. Points 4 and 5 are extremely important to the progress of the treatment.

4. Socialized speech activities
   (*a*) Purpose: to place stutterers in the situation which most nearly approximates a situation met in daily life
   (*b*) Procedures
      (1) Games
      (2) Club activities
   (*c*) Activities
      (1) Language games, such as Geography and Coffee Pot
      (2) Informal dramatizations
      (3) Pantomimes
      (4) Talks by the patients
      (5) Club work: children organized into a club in which all the activities are carried out by them with a minimum amount of supervision

VII. Therapeutic measures discussed with the parents:
   A. Knowledge gained in the talks with the child and with the parents to be utilized in the suggestions given to the parents on the handling of the child
   B. Parents generally advised:
      1. To ignore the child's defect
      2. To create harmonious and pleasant surroundings
      3. To give the child a feeling of security
   C. Adjustment of school problems, if any are found
   D. Correction of any physical defects

VIII. Periodic follow-up

IX. Program of treatment for the preschool child (group B)
   A. Interview with parents and therapy as outlined (I, II, III, IV, VII)
   B. Method of treatment
      1. More indirect approach than with the school child
         (1) Child not made conscious of his defect
         (2) Emphasis placed on the imitation of the good speech pattern set by the teacher
         (3) Parents to give child a good speech pattern, which is characterized by smoothness, fluidity and ease of initiation
   C. Intelligent cooperation of the parents stressed as an important factor in the therapy of the preschool child

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Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

CULTIVATION OF THE VIRUS OF LYMPHOCYTIC CHORIOMENINGITIS IN THE DEVELOPING CHICK EMBRYO. IDA A. BENGTSON and J. G. WOOLEY, Pub. Health Rep. **51**:29 (Jan. 10) 1936.

The virus of lymphocytic choriomeningitis was cultivated through eight passages in the chorio-allantoic membrane and in the brain of the chick embryo. The chick embryos inoculated with virus survived longer than mice inoculated with the virus, indicating greater resistance on the part of the embryo to the virus. The virus was present to approximately the same extent in the membrane and the brain of the embryo. It was also present in the liver and amniotic fluid. The lesion produced at the site of inoculation was relatively insignificant.

SANFORD, Chicago.

DEVELOPMENT CYCLE OF OXYURIS: ITS IMPORTANCE IN THE PRACTICE OF MEDICINE. GIUSEPPE PENSO, Policlinico (sez. prat.) **42**:1943 (Oct. 7) 1935.

There are a number of remedies capable of clearing the intestine of Oxyuris, but it is nevertheless by no means easy to effect a complete cure, for after an interval the parasites always return. It is not true that the victim reinfects himself with soiled hands, for oxyures are seldom found near the anus. The impregnated female keeps away from the anus. She is apparently insusceptible to pressure, and it is incorrect to speak of children badly infected with eggs of Oxyuris. It has long been known that the female Oxyuris often perforates the mucosa of the appendix and establishes herself in its wall. Photomicrographic observation shows that the female deposits her eggs beneath the mucosa. Here the embryo develops, and the early larval stage is passed within the intestinal wall, from which the worms enter the intestinal lumen. Consequently it is impossible to effect a cure by merely once driving them out of the intestine. This must be repeated three successive days at three week intervals, since this is the length of the Oxyuris cycle.

VINTON, New York.

A NEW MICROSEDIMETER. H. A. KANITZ, Deutsche med. Wchnschr. **61**:1929 (Nov. 29) 1935.

The inventor of a simple microsedimeter claims that the results obtained with his instrument check with those obtained with macromethods. One tenth of a cubic centimeter of blood is mixed with a 3.8 to 5 per cent solution of sodium citrate in proportion of 1:4 parts. This mixture is siphoned up in a fine graduated glass tube by means of a rubber stopper. The height of the column of blood is 20 cm., so the reading of the sedimentation of the blood is easy and convenient.

KERESZTURI, New York.

Metabolism; Infant Feeding; Milk and Other Foods

HYPOGLYCEMIA. A. F. HARTMANN, J. C. JAUDON and M. MORTON, J. Pediat. **11**:1 (July) 1937.

Over a period of fifteen years, 286 cases of hypoglycemia have been studied in the St. Louis Children's Hospital. Detailed histories of many of the cases are included in the report. These cases have been grouped and classified, a method

of classification being used which emphasizes the dominant position of insulin but which also recognizes other important etiologic factors. Classified as instances of true hyperinsulinism (excess of insulin) were cases of physiologic hyperactivity of the islands of Langerhans. Included in this group were cases of hypoglycemia following ingestion of large amounts of carbohydrate or following intravenous administration of dextrose, and cases in which the infant of a diabetic mother showed a greater fall of blood sugar shortly after birth than a normal infant sustains. Occasionally in such cases severe hypoglycemic manifestations develop, such as convulsions and collapse. The hypoglycemia in these cases seems referable to physiologic hyperactivity of the islands of Langerhans, due to the hyperglycemia of the maternal blood, rather than to hypertrophy or hyperplasia of the cells of the islets. The use of milk and carbohydrate feedings immediately after birth and of combined injections of epinephrine and dextrose when symptoms occur will prevent and control these symptoms. Histories of two cases of true hyperplasia and hypertrophy of the islands of Langerhans found at autopsy are included. The mother of only one of these babies was diabetic. Hypoglycemia following administration of insulin is discussed, both that in the diabetic and that in the athreptic infant.

Under the classification of relative hyperinsulinism are grouped cases in which there is deficient storage of glycogen due to starvation or to loss of carbohydrate from vomiting, diarrhea or fistula. In these instances the hypoglycemia results from a combination of diminished intake and increased utilization of food. Cases in which there are abnormalities of the liver with decrease in storage of glycogen belong in this group. Lack of development or breakdown of the carbohydrate metabolism may also be a cause of relative hyperinsulinism. To this group belong the cases found in new-born and premature infants. Hypoglycemia occurs regularly during the first four to five days of life and may be greatly intensified by hemorrhage into the adrenals or the brain. A large group of children suffering from relative hyperinsulinism are those who have recurring attacks of severe hypoglycemia, who seem to be hypersensitive to or intolerant of insulin, either because of the lack of proper opposing secretions from the adrenals or from the pituitary gland or because of lack of storage of glycogen in the liver. No case of adenoma or other pancreatic tumor occurred in this series, and since only one case in a child has been reported in the literature the condition must be extremely rare.

RAUH, Cincinnati.

EFFECT OF BOILING ON THE NUTRITIVE VALUE OF MILK. S. GRAHAM and N. MORRIS, Arch. Dis. Childhood **12**:169 (June) 1937.

The results recorded here indicate that there is no evidence that the boiling of milk over short periods impairs it either for absorption or for utilization when there is an ample supply of proximate principles and minerals and when the caloric intake is adequate. It still remains possible that over long periods, especially when the intake is no more than sufficient, the sterilization of milk might make a difference in the retention of essential substances. So far, however, satisfactory proof of this is lacking.

KELLY, Milwaukee.

A CASE OF EXTREME INFANTILE ATROPHY. O. DE ANDRADE FILHO, J. de pediat., Rio de Janeiro **4**:271 (July) 1937.

When first seen, the child was 9 months old and weighed 2,480 Gm. (1,320 Gm. less than its weight at birth). Over a period of four months an interesting study was made based on the daily weight of the foods given. The best gain and ultimate recovery were made on cow's milk with 5 per cent sugar, bananas, vegetables and cereal.

SANFORD, Chicago.

Vitamins; Avitaminoses

VITAMIN D IN CHILD HEALTH. F. O. TONNEY, Am. J. Pub. Health **26**:665 (July) 1936.

Tonney briefly summarizes present knowledge concerning the use of vitamin D in childhood, emphasizing its influence on growth, bone development, tooth development, posture and resistance to infection. He feels that vitamin D milk is of real value.

McBRYDE, Durham, N. C.

THE STORY OF THE VITAMINS IN INFANT NUTRITION. I. A. ABT, J. M. A. Georgia **26**:355 (July) 1937.

This is a historical review summarizing the practical application of the vitamins up to the present era. Their relation to deficiency diseases is clearly brought out.

MORRISON, Savannah, Ga.

EFFECT OF COOKING ON THE ANTISCORBUTIC VALUE OF VEGETABLES. L. F. LEVY, South African M. J. **11**:474 (July 10) 1937.

Using the chemical method for the quantitative determination of cevitamic acid, Levy found that the effect of cooking on vegetables is to bring about a loss in antiscorbutic value. The extent of the loss depends on various factors, as follows:

1. Amount of water used. In all cases, with the exception of unpeeled potatoes, a portion of the cevitamic acid is extracted by the boiling water; the larger the volume of water used, the greater the diffusion of the cevitamic acid.

2. Time of boiling. Since the cevitamic acid is slowly extracted during boiling, the longer the heating the greater is the loss.

3. Standing after boiling. When vegetables are allowed to stand for a long time after boiling, the cevitamic acid becomes fairly rapidly oxidized, presumably by atmospheric oxidation.

4. Presence of metallic substances. When vegetables are cooked in tinned or aluminum utensils, the loss in activity is not influenced by metal dissolved from the utensils.

5. Addition of alkalis. Solutions of cevitamic acid are rapidly destroyed by alkali, even when cold.

GONCE, Madison, Wis.

THE EXCRETION AND RETENTION OF CEVITAMIC ACID IN WOMEN AND CHILDREN. K. U. TOVERUD, Norsk mag. f. lægevidensk. **98**:441, 1937.

A study was made of the excretion of cevitamic acid in eight "normal" women, who showed an average daily excretion of 35.43 mg., with deviations from 15.8 to 53.9 mg. When they were given 250 mg. of cevitamic acid as orange juice, 50 per cent or more of the acid was excreted in the urine during the first twenty-four hours.

Ten normal children who were maintained on a commonly used diet did not show an average daily excretion of more than 11.9 mg. of cevitamic acid, with an excretion of from 13.5 to 43.8 per cent of a large test dose. After the children had been given for one week three oranges a day in addition to their common diet, the average daily excretion increased to 31 mg., and then they excreted during the first twenty-four hours 50 per cent of the test dose (from 200 to 300 mg.).

During different diseases the excretion was variable, dependent mostly on the amount of vitamin C taken in the food. When this was low, the daily excretion and the excretion after a large test dose were low; when the intake was high, the excretion was also high with three exceptions. Thus, of the sixteen children examined, five excreted 50 per cent of the test dose given. Six diabetic children receiving 200 Gm. of fresh fruit and 200 Gm. of vegetables daily had an average

daily excretion of 45 mg. The excretion after the test dose was above 50 per cent in two of them and between 30 and 50 per cent in the others.

In twelve pregnant women the daily excretion on an adequate diet was 19.1 mg. of cevitamic acid, with just a moderate increase of not up to 30 per cent after the test dose. The excretion following the test dose did not increase even after two additional oranges were given for one week. When, however, 250 mg. of cevitamic acid was given on successive days, an increase corresponding to that in adult but not pregnant women was seen on the fourth and fifth days.

In lactating women the average daily excretion was even lower, 13.3 mg., with hardly any increase following a test dose. In some of these women an increase in the excretion did not follow even after a daily intake of 250 mg. of cevitamic acid for five or six days.

During saturation of the organisms of lactating women, the content of cevitamic acid in the breast milk of one of these women increased up to 7.8 mg. per hundred cubic centimeters.

TOVERUD, Oslo, Norway.

Hygiene; Growth and Nutrition; Public Health

DIVERSE ATTRIBUTES OF HEALTHY CHILDREN: A REPORT OF PROGRESS IN UNDERSTANDING THE "NORMAL CHILD." A. H. WASHBURN, J. Pediat. **11**:37 (July) 1937.

Washburn describes the work which is being carried out by the Child Research Council. The council is making a longitudinal study of a group of one hundred average children of Denver. At regular intervals throughout the period of growth the following studies are made on each child: a complete physical examination; special examinations of the eyes, upper air passages, lungs, heart, bones, muscles and posture; a complete dental study; a complete anthropometric study; a study of the face and full length photographs; roentgen examinations of the head, heart, lungs, sinuses, teeth, long bones and joints; electrocardiographic studies; investigations of exercise tolerance and blood pressure, and determinations of the basal metabolic rate. Yearly check-ups of the child's intelligence quotient and of his behavior are made, as well as frequent visits to watch the child in his home environment. In addition, a number of studies of institutional babies and children and special pieces of research are being carried on. Illustrations of the type and character of the information which has been accumulated during the first five years of this study are presented.

RAUH, Cincinnati.

PUBLIC HEALTH METHODS IN A PRIVATE SCHOOL. L. P. SUTTON, J. Pediat. **11**:88 (July) 1937.

Sutton outlines the objectives of a health service in a private school and the function of the physician in carrying out these objectives. She describes the health program put into practice in a private day school for girls in New York City. She discusses in detail the management of immunization against diphtheria, the supervision of the health of school employees, the control of infections of the upper respiratory tract, the control of epidemics of contagious diseases and the correction of physical defects, with especial emphasis on the correction of poor posture.

RAUH, Cincinnati.

AN INVESTIGATION INTO THE HEALTH OF 1,530 PRE-SCHOOL CHILDREN. P. HENDERSON, Arch. Dis. Childhood **12**:157 (June) 1937.

During the period from January to July 1936, 1,530 preschool children were examined. Diseases and defects were noted and listed for each age group. Comment is made on the various disorders discovered.

KELLY, Milwaukee.

UNVEILING THE MYSTERY OF GROWTH. J. C. MEAKINS, M. J. Australia **1**:935 (June 19) 1937.

Concerning the stature of man Meakins concludes that, given normal pituitary and thyroid function, with a proper supply of vitamin B, amino-acids, ample food and physical exercise during the years between the ages of 5 and 20, the stature of a race may be increased to the optimum of Grecian perfection.

GONCE, Madison, Wis.

Prematurity and Congenital Deformities

PREMATURITY AS A PUBLIC HEALTH PROBLEM. M. GLEICH, New York State J. Med. **37**:947 (May 15) 1937.

In three municipal hospitals in New York City 990 premature infants were born, an incidence of 4.5 per cent. The rate was very high (8.24 per cent) in a hospital receiving patients from a district where the general health is low. Gleich recommends the establishment in the Central and East Harlem districts of a premature infant station equipped and modeled after the Cradle in Evanston.

AIKMAN, Rochester, N. Y.

PREMATURE INFANTS. W. W. WADELL, C. W. PURCELL and W. S. WRAY, South. M. J. **30**:535 (May) 1937.

The authors evaluate the various factors which make for success in the management of premature infants in the following order: (1) a nursing staff that is intelligent, enthusiastic and conscientious and an attending staff that has a special interest in premature infants, (2) measures for preventing thermal shock, (3) methods of feeding, (4) prevention of infection and (5) the physical equipment in the nursery.

SCHLUTZ, Chicago.

THE EARLY ANAEMIA OF PREMATURE INFANTS: THE HAEMOGLOBIN LEVEL OF IMMATURE BABIES IN THE FIRST HALF-YEAR OF LIFE AND THE EFFECT DURING THE FIRST THREE MONTHS OF BLOOD INJECTIONS AND IRON THERAPY. H. M. M. MACKAY, Arch. Dis. Childhood **10**:195 (June) 1935.

Observations were made at the Mothers' Hospital, London, on the hemoglobin level of one hundred and fifty infants during the first half year of life. The main object was to obtain information regarding the fall in the hemoglobin level during the first two or three months in babies of low weight at birth. Of the babies examined thirty-nine weighed less than 5 pounds (2,267 Gm.) at birth; fifty-two, from 5 to 6 pounds (2,267 to 2,721 Gm.), and fifty-nine, 6 pounds (2,721 Gm.) and more.

No influence on the extent of the decline in the hemoglobin level in the first two or three months of life was observed as a result of an intramuscular injection of 15 cc. of citrated human blood within the first three days of life or from the administration of iron and ammonium citrate by mouth.

Values are given for the average hemoglobin level during the first six months of life of babies weighing at birth 3, 4 and 5 pounds (1,366, 1,822 and 2,267 Gm.), respectively. In none of these babies did the hemoglobin concentration drop below 63 per cent. The infants weighing 3 and 4 pounds started with a higher hemoglobin level than those weighing 5 pounds but from the eighth to the twenty-second day the levels for the first group were consistently slightly lower than those for the larger babies. Babies showing symptoms of any severe pathologic condition in the early weeks of life were excluded from these groups. It is suggested that premature and immature babies whose general health and progress have been satisfactory from birth do not usually show severe anemia during the first three months of life. The mechanism which brings about an excessive decrease

in the amount of hemoglobin remains unexplained; possibly excessive hemolysis, diminished production of red cells and hydremia may all play their part in varying degree.

KELLY, Milwaukee.

CONGENITAL MALFORMATION OF THE LARGE BOWEL. J. ALEXANDER MACKENZIE, Brit. M. J. **2**:61 (July 13) 1935.

A case is reported of extensive malformation of the large bowel, evidently of congenital origin, in a man, aged 42. The author explains the deformity on the basis of the embryologic development.

ROYSTER, University, Va.

ACRODYSPLASIA. TYPE: SYNDACTYLIC OXYCEPHALY. DAVID M. GREIG, Edinburgh M. J. **42**:537 (Oct.) 1935.

Greig writes again of cranial malformations and supplies excellent drawings of the deformities of a patient. Nine years ago his work on oxycephaly was abstracted for this journal. He then differentiated between true and false oxycephaly. In the current communication he discusses the association of general somatic conditions with the cranial deformities and the possible causes therefor.

The history of the patient from infancy to old age is related. The drawing of the patient shows the woman in advanced life. The observations at autopsy are given. Greig points out that in the infant and child the bones are incompletely formed, so that the constituents of the skull characteristic of this condition can only be surmised. The patient showed a striking symmetry in the bilateral condition of the hands and feet. The skull is hypsocephalic; the face is not affected as it is in true oxycephaly. The cranial deformities and the syndactylism are manifestations of acrodysplasia. Greig believes that in such congenital malformations as acrodysplasia, when similar constituents of distant parts of the body are synchronously affected, one can assume that the body has been subjected to a general influence, probably resembling a hormone, which causes excessive or retarded specific cellular activity.

This communication, along with the aforementioned earlier one, greatly aids in the recognition of types of high skulls and the differentiation between true and false oxycephaly.

SPECIMEN FROM A CASE OF ABSENCE OF CEREBRAL HEMISPHERES IN WHICH THE INFANT SURVIVED FOR TWO WEEKS. DAVID HALER, Proc. Roy. Soc. Med. (Sect. Dis. Child.) **28**:1075 (June) 1935.

The past history and the results of physical examination of the infant on admission to the hospital and of postmortem examination are reported.

WILLIAMSON, New Orleans.

MALFORMATION OF THE UPPER PORTION OF THE STOMACH IN AN INFANT. R. TURQUETY and M. MIGNON, J. de méd. de Paris **24**:525 (June 13) 1935.

A boy, 13 months old, had a history of repeated vomiting from birth. Since the age of 4 months the vomitus had frequently contained blood. The child was malnourished, and there was definite anemia. A roentgenogram showed a ball-like dilatation in the region of the cardia, with restriction below. Some lessening of the vomiting was obtained with thickened food. Injections of an extract of liver and amino-acids were also given for relief of the anemia.

LESLIE, Evanston, Ill.

ANUS VESTIBULARIS, OR FISTULA RECTOVESTIBULARIS, DIAGNOSED DURING LABOR. IWAN DE OLIVEIRA FIGUEIREDO, Rev. de gynec. e d'obst. **29**:283 (June) 1935.

The author describes a case of this condition, which he encountered at the delivery of a woman aged 24. It caused considerable difficulty in delivery, which

was successfully accomplished. He thinks that this anomaly should be repaired in infancy. It occurs in about 1 in 10,000 persons. There is usually a family history of stigma, such as syphilis, alcoholism or tuberculosis. Embryologically it is a defect of the cloaca. Clinically there is usually incontinence of feces. The treatment is surgical and depends on the extent of the deformity.

SANFORD, Chicago.

MALFORMATIONS OF THE ESOPHAGUS. A. NAGEL, Monatschr. f. Kinderh. **61**:401, 1935.

A case of a congenital malformation of the esophagus is reported, illustrated by a diagram. The upper portion of the esophagus ended blindly a little above the second thoracic vertebra. The lower portion extending upward from the stomach ended with a fistula into the trachea above the bottom of the upper segment.

A gastrostomy was done, and the infant was kept alive for three months. An interesting feature of the case was the fact that when barium sulfate was introduced through the gastrostomy opening a roentgenogram showed a shadow in the upper part of the esophagus.

Postmortem examination showed that the contrast medium introduced into the stomach was probably regurgitated upward into the trachea, then coughed up to the throat and swallowed into the blind esophageal pouch.

GERSTLEY, Chicago.

INTRA-UTERINE FRACTURES: REPORT OF TWO CASES. H. J. HARTENSTEIN, Monatschr. f. Kinderh. **70**:77 (April) 1937.

Two cases of intra-uterine fracture of both bones of the lower part of the leg are reported in new-born infants. In most of these cases the fracture is at about the union of the middle and the lower third, with the convexity forward. Sometimes there is a scar in the skin at this point suggestive of intra-uterine pressure. Children with such fractures may have deformities of the toes and also of the fibula. A photograph and roentgenograms portray this deformity excellently.

GERSTLEY, Chicago.

Acute Contagious Diseases

THE HEART FIFTEEN TO TWENTY YEARS AFTER SEVERE DIPHTHERIA. W. P. THOMPSON, S. E. GOLDEN and P. D. WHITE, Am. Heart J. **13**:534 (May) 1937.

About 100 persons who had severe or moderately severe diphtheria from fifteen to twenty years ago no proof was obtained of disturbed conduction developing years after the illness.

GIBSON, Chicago

DIPHTHERIA SIMULATING PERITONSILLAR ABSCESS: DANGERS OF INCISION. A. H. NEFFSON and J. BREM, Arch. Otolaryng. **25**:260 (March) 1937.

The authors call attention to the fact that clinically diphtheria may sometimes be easily mistaken for peritonsillar abscess, an error which often proves disastrous. Six such cases are discussed (three of them fatal), with proof based on electrocardiographic and autopsy observations. Two of the patients showed toxic myocarditis. Each of the patients was under medical supervision before admission to the hospital. The fatal outcome in these cases is due to failure to recognize the condition. The safe procedure when there is a peritonsillar abscess is to make bacterial cultures in order to rule out diphtheria.

GREENWOOD, Chicago.

GOLD TRIBROMIDE IN THE TREATMENT OF PERTUSSIS. J. EPSTEIN, Arch. Pediat. **54**:177 (March) 1937.

From a comparison of the therapeutic results in children with whooping cough treated with gold tribromide and the results in those treated by other methods the author states that the duration of the disease is reduced to almost one-third when gold tribromide is used. The average duration of the disease in 250 children treated with gold tribromide was three and eight-tenths weeks, while in the group of 100 children treated by other methods it was ten weeks. ORR, Buffalo.

PRESENT STATUS OF SERUM THERAPY IN PEDIATRICS. J. H. HESS, Arch. Pediat. **54**:251 (May) 1937.

The present status and value of serum in the treatment of communicable and infectious diseases are discussed. ORR, Buffalo.

USE OF PLACENTAL GLOBULIN TO PREVENT AND MODIFY MEASLES. J. M. JOSEPH and M. GLEICH, Arch. Pediat. **54**:307 (May) 1937.

In an attempt to prevent measles fifty-six children were given placental extract. Fifty (90 per cent) were completely protected. Five children contracted mild measles with no complications. The remaining child had an average attack of the disease. The factors which govern the dose of placental extract are: (1) intimacy of exposure, (2) number of days after exposure and (3) desirability of prevention or of modification of the disease. ORR, Buffalo.

MENINGOCOCCEMIA WITHOUT MENINGITIS. F. W. GOUNDRY and T. H. PHALEN, New York State J. Med. **37**:491 (March 1) 1937.

A white boy aged 14 complained of fever, chills, headache, pain in the joints and mental apathy. This was followed by profuse sweating and a generalized rash resembling that of typhoid. Meningococci were present in the culture of the blood. He had no cerebrospinal symptoms. Antimeningococcus serum was given intramuscularly, and the boy made a good recovery. AIKMAN, Rochester, N. Y.

SULPHANILAMIDE, SERUM, AND COMBINED DRUG AND SERUM THERAPY IN EXPERIMENTAL MENINGOCOCCUS AND PNEUMOCOCCUS INFECTIONS IN MICE. S. E. BRANHAM, Pub. Health Rep. **52**:685 (May 28) 1937.

Sulfanilamide showed marked therapeutic action in mice in which a meningococcic infection had been produced experimentally. Twenty strains of types I, II and III of meningococci were used. The drug was more effective when administered subcutaneously than when by mouth. The drug was more effective than serum. A combination of serum and drug therapy yielded much better results than either alone. A synergistic action seemed to exist. The same results were obtained with pneumococci of type I. The results obtained indicate that combined drug and serum therapy in meningococcic and pneumococcic infections in man is worthy of trial. SANFORD, Chicago.

THE PREVENTION OF DEATHS FROM MEASLES. H. WILLIAMS, South. M. J. **30**:304 (March) 1937.

There is no practical agent for immunization against measles. The school age, from 5 to 14 years, is the safest period in which the child may have measles, as death from the disease is rare at that age. Measles is a serious danger to a child under 3 years of age. The prevention of deaths, therefore, is an age-specific problem of considerable importance. SCHLUTZ, Chicago.

Ocular Paralyses After Mumps. T. Harrison Butler, Brit. M. J. **1**:752 (April 10) 1937.

Two cases of mumps are reported in which ocular complications or manifestations were demonstrated. Butler thinks that a meningeal reaction is present in most cases of this disease, even in the absence of any symptoms or signs indicative of cerebral involvement. He thinks that the virus of mumps is potentially neurotropic. There are other paralyses which affect various nerves and nerve trunks.

Royster, University, Va.

Immunization Against Diphtheria with Alum-Precipitated Toxoid. George Chesney, Brit. M. J. **1**:807 (April 17) 1937.

It is evident from this article that the author performs immunization with from 0.1 to 0.2 cc. in the first dose, followed by 0.4 cc. four weeks later. The Schick test is given two months later, and in this case only one child gave a positive reaction.

Royster, University, Va.

Post-Scarlatinal Nephritis. B. A. Peters and Iris M. Cullum, Brit. M. J. **1**:1020 (May 15) 1937.

The authors present a discussion on the prevention of postscarlatinal nephritis by the administration of (*a*) large amounts of alkalis in the course of an attack of scarlet fever and (*b*) thyroid and iodine. Their results were controlled but are not conclusive; apparently no account is taken of the well known seasonal differences in the incidence of complications in this condition, as well as in other infectious diseases.

Royster, University, Va.

A Note on the Prophylaxis of Chickenpox. J. W. Bigger, Irish J. M. Sc., March 1937, p. 126.

The author took some vesicle fluid from a patient with chickenpox and injected it intradermally into the arm of a nonimmune person who had been exposed to the patient two days previously. A vesicle developed at the site of the injection, but there were no further complications.

Snelling, Toronto, Canada.

Effect of Mumps on the Wassermann Reaction. W. Smith, Lancet **1**:754 (March 27) 1937.

The case of a 3 year old child is cited to show the importance of remembering that the Wassermann test as normally performed, using a nonspecific antigen, may lead to a wrong diagnosis. The chief complaint on admission was weakness and lethargy. The Wassermann tests of the blood and spinal fluid were positive. The diagnosis of syphilitic encephalitis was suggested.

Another child aged 5 years also gave a weakly positive Wassermann reaction of the blood. The Wassermann reactions of both parents were negative.

Further questioning revealed that both children had had mumps six weeks previously, and the diagnosis of encephalitis following mumps thus became clear. The patient's condition rapidly deteriorated and he died, but no postmortem examination was performed.

The surviving child's Wassermann test, done four months later, was negative.

Langmann, New York.

Diphtheritic Myocarditis. N. D. Begg, Lancet **1**:857 (April 10) 1937.

Early Circulatory Failure.—This appears within the first few days of the disease and represents the sum of toxic effects on all organs. The principal clinical manifestations are a fall in blood pressure, a small rapid pulse, extreme pallor, cyanosis and coldness of the extremities. The carbohydrate metabolism is

invariably deranged, and there is abnormal body response to intravenous injection of dextrose, in the direction of a higher level of sugar in the blood. Electrocardiographic evidence of myocarditis may or may not be present but is rarely so pronounced as to indicate impending death—an event which frequently ensues.

Late Circulatory Failure.—This appears usually between the third and fourteenth days of the disease. Evidence of peripheral failure may be present, but the outstanding feature is clinical and electrocardiographic evidence of damage to the heart muscle or to the specialized tissue of the conducting system. Death is also a common event in late circulatory failure, but almost any degree of myocardial damage may be reasonable in individual cases, and on the whole the outlook is relatively better than in early circulatory failure.

Investigation of a series of 100 cases of severe diphtheria showed that in the great majority cardiac abnormalities developed within the first three weeks of the disease. In many cases the exact nature of the abnormality could not be recognized except by the auxiliary evidence of an electrocardiogram.

If complete heart block, bundle branch block or paroxysmal tachycardia appears in the electrocardiogram during the course of diphtheria, the outlook as regards recovery is relatively bad.

In the presence of other evidence of myocardial involvement, including intraventricular block, the prognosis is reasonably favorable.

A normal electrocardiogram, particularly within the first few days of the disease, does not preclude sudden circulatory collapse.

Except in a small proportion of conductive lesions, recovery after diphtheritic myocarditis appears to be complete as judged by electrocardiograms taken in convalescence.

LANGMANN, New York.

MENINGITIS FROM CHICKENPOX. E. IMBASSAHY, J. de pediat., Rio de Janeiro **4**:173 (May) 1937.

An 8 year old boy presented convulsions, high temperature and unconsciousness five hours after the eruption of chickenpox. Later typical meningitic symptoms were shown. These were so severe that meningitis was considered, but the spinal fluid showed only 15 leukocytes per millimeter. Recovery was uneventful.

SANFORD, Chicago.

ATYPICAL POLIOMYELITIS. E. FILGUEIRAS, J. de pediat., Rio de Janeiro **4**:199 (May) 1937.

A girl 2 years old was presumed to be suffering from syphilitic paralysis.

SANFORD, Chicago.

HISTOLOGIC DIAGNOSIS OF MEASLES. C. WEGELIN, Schweiz. med. Wchnschr. **67**:1, 1937.

The Warthin-Finkeldey giant cells were found in the germ centers, neighboring lymphatic tissue and tunica propria of the mucosa of the vermiform appendix removed surgically from each of three patients during the prodromal stage of measles. The giant cells were round or oval, often measured over 100 microns in diameter and contained from 50 to 100 chromatin-rich nuclei, which frequently were found undergoing pyknosis and karyorrhexis. Ingested lymphocytes and nuclear fragments were present in the protoplasm of these cells. In one case the mesenteric lymph nodes showed a primary tuberculous infection, with central caseation and calcification, surrounded with large epithelioid cells and Langhans giant cells, while the rest of the lymph nodes revealed giant cells similar to those seen in the appendix. The Warthin-Finkeldey giant cells indicate a reaction to infection by the virus of measles. The frequent localization in the appendix suggests that this organ may be a portal of entry for the virus, which then spreads to the mesenteric lymph glands.

STENN, Chicago. [ARCH. PATH.]

PARALLERGIC VACCINAL EXANTHEM. R. BRANDT, Wien. klin. Wchnschr. **50**:369 (March 19) 1937.

Atypical reactions following vaccination against smallpox include those which depend on a specific allergic reaction (so-called parallergic symptoms).

Brandt describes the case of a 7 year old boy inoculated against smallpox who after ten days manifested a rash clinically similar to erythema multiforme. About two days later a new eruption with the general characteristics of a toxic urticarial multiform exanthem appeared.

The interval of ten days practically precludes the vaccine as the direct cause of the eruptions. Also, the evidence seems to rule out antibodies of the blood as having any important relation to smallpox vaccine. Finally, a strictly allergic reaction would have occurred sooner and appeared in the form of typical vaccine pustules.

The author believes that the exanthem occurred as a reaction to a nonspecific counterirritant present during the development of the vaccine-induced allergy. Identification of this third factor is aided by the knowledge that angina developed shortly after the vaccination.

Thus, the postvaccinal exanthem is to be considered a reaction of an organism made allergic by the vaccine to a parallergic antigen in the form of the cocci of the angina.

Brandt recommends the use of Keller's term "parallergic vaccinal exanthem" in place of the commonly used "postvaccinal exanthem" in describing a condition of this type.

ABT, Chicago.

VACCINATION AGAINST SMALLPOX. I. HOLMGREN and B. LINDSTRÖM, Acta med. Scandinav. **91**:610, 1937.

Five hundred and thirteen persons were vaccinated on admission to the hospital, and it was established that illness does not constitute any risk or contraindication to vaccination.

One-half the persons who had been vaccinated forty or more years before were still immune, but 10 per cent had lost their immunity within ten years.

Older persons who were revaccinated had more violent reactions than the younger patients provided that the same number of years had passed since the first vaccination, indicating that the immunity obtained in childhood is more persistent.

KAJDI, Baltimore.

Acute Infectious Diseases

THE MECHANISM OF IMPAIRED AURICULOVENTRICULAR CONDUCTION IN ACUTE RHEUMATIC FEVER. HOWARD G. BRUENN, Am. Heart J. **13**:413 (April) 1937.

Impairment of auriculoventricular conduction is common during the course of acute rheumatic fever. This disturbance has been attributed to: (1) anatomic change involving the auricles and the bundle of His, (2) the direct effect of toxins on the conduction system and (3) heightened vagal action or an increased response to vagal control under the influence of the toxins of the infections.

An attempt is made to analyze the mechanism of this disturbance. Twenty-two patients with acute rheumatic fever were studied. Each showed impairment of auriculoventricular conduction. Atropine sulfate was administered intravenously. In nineteen of the twenty-two patients studied, the conduction defect was completely abolished. The effect was always transient. Bruenn concluded that in cases of acute rheumatic fever, impairment of auriculoventricular conduction is due, in part at least, to an increase in the vagal tone.

GIBSON, Chicago.

INVASION OF THE SUBMUCOSA OF THE HUMAN SMALL INTESTINE BY ANCYLOSTOMA BRAZILIENSE. C. BONNE, Am. J. Trop. Med. **17**:587 (July) 1937.

Bonne reports five cases of infection of the submucosa of the human small intestine by Ancylostoma braziliense and describes the worms, larvae, ova and lesions produced by the parasite.

He states that the filariform larva of this worm behaves in an erratic manner when it invades the human skin, wandering about and producing a creeping eruption. After reaching the intestinal tract and developing to maturity, it continues to wander in search of a more suitable location. The author believes that this is why it invades the intestinal wall, where it produces considerable damage in the form of local hemorrhages and inflammation characterized by eosinophilia.

BURPEE, Augusta, Ga.

AN OUTBREAK OF TRICHINIASIS IN CENTRAL OHIO AND THE USE OF THE BACHMAN INTRADERMAL SKIN TEST. AUGUSTUS A. HALL, Ann. Int. Med. **10**:1544 (April) 1937.

Eight cases of trichiniasis are reported in which the patients recovered. Three of these occurred in children. A description of the antigen and of the technic for its use is given. The antigen is not available commercially at present. The Bachman intradermal test is considered a reliable diagnostic aid in trichiniasis and should supplant biopsy of a sypecimen of muscle. READING, Galveston, Texas.

A BACTERIOLOGICAL STUDY OF FORTY CASES OF DYSENTERY IN INFANTS AND CHILDREN, INCLUDING TWO CASES OF FLEXNER BACILLUS SEPTICEMIA. EDITH HAYNES, J. Infect. Dis. **60**:251 (March-April) 1937.

Haynes studied forty cases of dysentery in children. She obtained the Flexner bacillus in thirteen cases, including two in which it was obtained from the blood stream. The Sonne dysentery bacillus was isolated in five cases. Haynes thought that the reason the Sonne dysentery bacillus was not isolated in more cases was that the infection in such cases is usually mild and the patient is not hospitalized. She concluded that if the titer is not over 1:100 the agglutination reaction is of doubtful value for diagnosis. JOHN A. TOOMEY, Ceveland.

POTENCY OF TYPHOID AND PARATYPHOID VACCINES WHEN FRESHLY PREPARED AND AFTER STORAGE. L. MISHULOW, I. MOWRY and A. K. STOCKER, J. Infect. Dis. **60**:356 (May-June) 1937.

Potent typhoid and paratyphoid vaccines may be stored for several years without demonstrable loss of potency. TOOMEY, Cleveland.

QUANTITATIVE CAPSULE SWELLING TESTS IN BLOOD SERUM OF PNEUMONIA PATIENTS. J. G. M. BULLOWA and J. SHARFF, J. Infect. Dis. **61**:55 (July-Aug.) 1937.

The antibody causing swelling of the capsules of pneumococci appears in the serum when pneumonic patients recover. Clapp's method for the quantitative determination of the "capsule swelling" substance is described. The amount of "capsule swelling" antibody present in the blood of pneumonic patients recovering, either spontaneously or after the injection of specific serum, may be determined, provided serum of known mouse protection titer and fresh cultures of pneumococci with good capsules are available. The results obtained by this method paralleled the amounts of protective antibody estimated by the more costly and time-consuming mouse protection tests.

A patient with fatal pneumonia due to Pneumococcus type II had, simultaneously, bacteremia and "capsule swelling" antibody. Because bacteremia may be present coincidently with capsule swelling and agglutination in patients suffering from pneumonia caused by Pneumococcus type II, these two phenomena are not satisfactory guides as to the adequacy of treatment. TOOMEY, Cleveland.

THE NATURAL HISTORY OF RHEUMATIC FEVER IN THE FIRST THREE DECADES. MAY G. WILSON, J. Pediat. **10**:456 (April) 1937.

This is a report of a twenty year period of observation on the course of rheumatic fever in 337 subjects, 225 of whom had lived to ages of from 16 to 30 years at the time of the report and 112 of whom had died of the disease. The onset of the disease from childhood is characterized by protean manifestations of activity and by a varied number of years of freedom from recurrence or by continuous years of manifestation of active infection. After puberty, at about the age of 16 years, 66 per cent of the subjects were free from recurrence of symptoms as compared with the 13 per cent before this period.

The disease appears to be self-limited, death being due in most cases to active carditis. The first attack of carditis may be fatal, but the majority of the deceased subjects survived subsequent attacks. The average age at which death occurred was 12.6 years, and the greatest incidence of death was in the group from 12 to 16 years of age inclusive.

The type of rheumatic manifestation, exclusive of active carditis, did not appear to be of prognostic significance. The incidence of cardiac disease was comparable whether the patients exhibited pains in the joints alone or chorea or polyarthritis with or without pains in the joints. All of the subjects presented evidence of cardiac involvement, although in only 39 per cent were the symptoms of carditis above the clinical horizon and capable of recognition, and in these patients the amount of cardiac damage was greater and the mortality was higher.

During the course of the disease physical signs of valvular involvement may disappear or may be inconstant or uncharacteristic and lead to the erroneous opinion that the heart is undamaged. The presence of considerable cardiac enlargement, established only by roentgenographic examination, indicates the limitation of a diagnosis of the absence of cardiac involvement in rheumatic persons based on physical examination alone. The majority of those who survived were able to carry on their work without circulatory symptoms, particularly after puberty. The author feels that the usual unfavorable prognostic opinion that the majority of rheumatic patients die during the third and fourth decades may be erroneous and that a further period of observation of these patients is necessary before a final comment is given.

RAUH, Cincinnati.

FORMOL-TOXOIDS IN THE PROPHYLAXIS OF GAS GANGRENE. W. J. PENFOLD and J. C. TOLHURST, M. J. Australia **1**:982 (June 26) 1937.

The authors found that formaldehyde toxoids of Bacillus Welchii (toxin digested with solution of formaldehyde) and suspensions of alum precipitates of similar formaldehyde-toxoids produce effective immunity in mice, rats and guinea-pigs.

GONCE, Madison.

TYPHOID ENDOTOXOID IMMUNIZATION IN CLOSED EUROPEAN COMMUNITIES. J. J. DE VILLIERS, South African M. J. **11**:221 (April 10) 1937.

Basing his opinion on results among 5,664 persons, de Villiers regards typhoid endotoxoid vaccine as superior to any other method of immunization against typhoid.

GONCE, Madison, Wis.

DYSENTERY IN INFANCY. MAHAMMED ALI, J. Egyptian M. A. **20**:167 (April) 1937.

This article is a report on the cultures of the stools of 139 infants of less than 2 years of age, suffering from dysentery (86) or simple diarrhea (53). Identification of the cause was possible in 75 of the 86 cases of dysentery. The incidence of Bacillus dysenteria Flexner was the highest (29.9 per cent), with Bacillus paracoli (15.1 per cent) and Bacillus Morgani No. 1 (11.6 per cent) next in order. Organisms were grown or parasites were isolated in 12 of the 53 cases of simple diarrhea.

MULHERIN, Augusta, Ga.

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QUANTITATIVE CAPSULE SWELLING TESTS IN BLOOD SERUM OF PNEUMONIA PATIENTS. J. G. M. BULLOWA and J. SHARFF, J. Infect. Dis. **61**:55 (July-Aug.) 1937.

The antibody causing swelling of the capsules of pneumococci appears in the serum when pneumonic patients recover. Clapp's method for the quantitative determination of the "capsule swelling" substance is described. The amount of "capsule swelling" antibody present in the blood of pneumonic patients recovering, either spontaneously or after the injection of specific serum, may be determined, provided serum of known mouse protection titer and fresh cultures of pneumococci with good capsules are available. The results obtained by this method paralleled the amounts of protective antibody estimated by the more costly and time-consuming mouse protection tests.

A patient with fatal pneumonia due to Pneumococcus type II had, simultaneously, bacteremia and "capsule swelling" antibody. Because bacteremia may be present coincidently with capsule swelling and agglutination in patients suffering from pneumonia caused by Pneumococcus type II, these two phenomena are not satisfactory guides as to the adequacy of treatment. TOOMEY, Cleveland.

THE NATURAL HISTORY OF RHEUMATIC FEVER IN THE FIRST THREE DECADES. MAY G. WILSON, J. Pediat. **10**:456 (April) 1937.

This is a report of a twenty year period of observation on the course of rheumatic fever in 337 subjects, 225 of whom had lived to ages of from 16 to 30 years at the time of the report and 112 of whom had died of the disease. The onset of the disease from childhood is characterized by protean manifestations of activity and by a varied number of years of freedom from recurrence or by continuous years of manifestation of active infection. After puberty, at about the age of 16 years, 66 per cent of the subjects were free from recurrence of symptoms as compared with the 13 per cent before this period.

The disease appears to be self-limited, death being due in most cases to active carditis. The first attack of carditis may be fatal, but the majority of the deceased subjects survived subsequent attacks. The average age at which death occurred was 12.6 years, and the greatest incidence of death was in the group from 12 to 16 years of age inclusive.

The type of rheumatic manifestation, exclusive of active carditis, did not appear to be of prognostic significance. The incidence of cardiac disease was comparable whether the patients exhibited pains in the joints alone or chorea or polyarthritis with or without pains in the joints. All of the subjects presented evidence of cardiac involvement, although in only 39 per cent were the symptoms of carditis above the clinical horizon and capable of recognition, and in these patients the amount of cardiac damage was greater and the mortality was higher.

During the course of the disease physical signs of valvular involvement may disappear or may be inconstant or uncharacteristic and lead to the erroneous opinion that the heart is undamaged. The presence of considerable cardiac enlargement, established only by roentgenographic examination, indicates the limitation of a diagnosis of the absence of cardiac involvement in rheumatic persons based on physical examination alone. The majority of those who survived were able to carry on their work without circulatory symptoms, particularly after puberty. The author feels that the usual unfavorable prognostic opinion that the majority of rheumatic patients die during the third and fourth decades may be erroneous and that a further period of observation of these patients is necessary before a final comment is given.

RAUH, Cincinnati.

FORMOL-TOXOIDS IN THE PROPHYLAXIS OF GAS GANGRENE. W. J. PENFOLD and J. C. TOLHURST, M. J. Australia **1**:982 (June 26) 1937.

The authors found that formaldehyde toxoids of Bacillus Welchii (toxin digested with solution of formaldehyde) and suspensions of alum precipitates of similar formaldehyde-toxoids produce effective immunity in mice, rats and guinea-pigs.

GONCE, Madison.

TYPHOID ENDOTOXOID IMMUNIZATION IN CLOSED EUROPEAN COMMUNITIES. J. J. DE VILLIERS, South African M. J. **11**:221 (April 10) 1937.

Basing his opinion on results among 5,664 persons, de Villiers regards typhoid endotoxoid vaccine as superior to any other method of immunization against typhoid.

GONCE, Madison, Wis.

DYSENTERY IN INFANCY. MAHAMMED ALI, J. Egyptian M. A. **20**:167 (April) 1937.

This article is a report on the cultures of the stools of 139 infants of less than 2 years of age, suffering from dysentery (86) or simple diarrhea (53). Identification of the cause was possible in 75 of the 86 cases of dysentery. The incidence of Bacillus dysenteria Flexner was the highest (29.9 per cent), with Bacillus paracoli (15.1 per cent) and Bacillus Morgani No. 1 (11.6 per cent) next in order. Organisms were grown or parasites were isolated in 12 of the 53 cases of simple diarrhea.

MULHERIN, Augusta, Ga.

RHEUMATIC DISEASE IN CHILDHOOD. H. GRENET, Arch. de méd. d. enf. **40**:329 (June) 1937.

A ten year study of 240 patients with rheumatism and 112 patients with chorea, of which previous reports have been made, is now completed. With respect to the frequency of rheumatism in early life it was found that the number of very young patients approximated 1.93 per cent of the total number admitted, including those hospitalized for contagious diseases. The percentage of patients with chorea during the second five year period of life was 0.7 as compared with 3.06 reported by Besnier in 1869.

Contrary to the observations of many clinicians, it was found that rheumatism is a disease of all seasons, at least in the climate of Paris, with two periods of maximal incidence, the first continuing through January and February and the second through June and July. The influence of age was well marked; only 2 patients were 3 years old or less, and only 4 were under the age of 5, but the number of patients older than this rapidly increased up to the age of 15. Sex appeared to exert no special influence in the development of rheumatic disease. In discussing the question of contagion, Grenet states that there may be some basis for the assertion that the commonly noted appearance of these disorders in several members of a family establishes them among the communicable diseases. The theory that such conditions may be tuberculous is discounted, but the influence of scarlet fever as an etiologic factor in many cases is supported.

An exhaustive clinical study, based on observations of the two series, concludes the monograph.

AMESSE, Denver.

ANNULAR ERYTHEMA AND STREPTOCOCCEMIA IN THE COURSE OF BOUILLAUD'S DISEASE. R. DEBRÉ, M. LAMY and M. L. JAMMET, Arch. de méd. d. enf. **40**:357 (June) 1937.

Six cases of annular and marginated erythema in children suffering from acute articular rheumatism are reported. In two of the patients, blood cultures revealed the presence of Streptococcus viridans and demonstrated the relation between Bouillaud's disease and malignant endocarditis of the retarded type.

Cutaneous eruptions in the course of acute rheumatic disease of childhood have been recognized since Rayer, in 1833, recorded his classic observations. They may occur early in the invasion, preceding by several days the articular or cardiac symptoms. The parts involved include the thorax, abdomen, loins and, less frequently, the neck and limbs; the face and the mucous membranes are always spared. The eruption is usually very light and may easily be overlooked; it appears, spreads and disappears in a few hours, so that the topography of the rash is continually changing. The color varies from lilac to copper and disappears on pressure; as the rash extends, the center of the pattern becomes pale, while the periphery shows a more intense discoloration, giving the typical ringlike appearance described by the Viennese school. There is neither itching nor desquamation. The only disorders which might confuse one in diagnosis are the so-called fifth disease and infectious erythema.

AMESSE, Denver.

CLINICAL TYPES OF RHEUMATIC INFECTION IN CHILDHOOD. E. A. GORNITZKAZA, Arch. de méd. d. enf. **40**:368 (June) 1937.

More intensive inquiry into the pathogenesis of acute articular rheumatism seems to have established it definitely as a cardiovascular disease. The investigations of Aschoff have been extended by numerous observers, and nodules of the type described first by him are accepted generally as specific for this disease. The studies of Talalayeff and others show that rheumatism is primarily a cardiac disease, in which articular involvement may or may not supervene. Particularly in the variety of endocarditis developing during the course of chorea, the articulations are apt to be found immune from attack. Anatomopathologic research has also proved that in this infection not only is the heart affected but the arteries as well; Zuckerstein suggested the name "cardio-arterial rheumatism" instead of

the present designation, "polyarthritic rheumatism." In this connection the sage observation of Lasègue is recalled: "Rheumatism licks the articulations but eats the heart." Although the pathology may be thus elucidated, the etiology is not so readily cleared up. While most authorities admit rheumatism into the category of infections, there is considerable dispute concerning the identification of the infective organism. All agree, however, that it is a special variety of the streptococcus.

A review of 620 cases of rheumatism in children includes very extensive discussion of the three common types: acute articular rheumatism; cardiac rheumatism without participation of the articulations, and rheumatism of the nervous variety (chorea), with illustrative cases under each head. The author emphasizes repeatedly the opinion that rheumatism, like tuberculosis, is essentially a disease of childhood and requires as intensive efforts in prophylaxis.

AMESSE, Denver.

PREVENTION OF ACUTE ARTICULAR RHEUMATISM. E. LESNÉ and J. A. LIÈVRE, Bull. Assoc. internat. de pédiat. prévent. **4**:3, 1937.

Acute articular rheumatism (Bouillaud's disease) is a specifically infectious illness.

The chief preventive measures are good housing, proper food and care of the gums, teeth, nose and pharynx. The infection seems to coincide with throat trouble. Isolation of all patients with quinsy and other acute inflammations of the throat would doubtless lessen the frequency of articular rheumatism.

Prolonged and repeated treatment with salicylic acid helps in preventing relapses.

AMESSE, Denver.

GLANDULAR FEVER. JULIO C. SANTA MARIA and JUAN C. PICENA, Rev. Soc. de pediat. de Rosario **2**:3 (April) 1937.

While reporting two cases of glandular fever (infectious mononucleosis) in patiens who were kept under observation until recovery, Santa Maria and Picena take the opportunity to warn their colleagues against the error of making a diagnosis of leukemia without repeated observations of the hemogram. They plead, too, for careful hematologic study of all patients presenting the clinical features of glandular fever so that epidemic foci may be recognized. They express the opinion that, in retrospect, it may be said that an unrecorded epidemic of glandular fever probably occurred during 1936 in the vicinity of Rosario.

KALISKI, San Antonio, Texas.

HEPATITIS EPIDEMICA. P. SELANDER, Kinderärztl. Praxis **8**:250 (June) 1937.

From a review of recent conceptions concerning catarrhal jaundice the author finds that there have been epidemics all over the world. In Sweden this disease must be reported to the health department. Catarrhal jaundice occurs throughout the year but has a definite seasonal predilection for the fall and winter months. It affects mainly children and young adults, without favoring one special sex. Syphilis predisposes to this disease. Several authors believe that the so-called syphilis and neoarsphenamine icterus is more or less identical with catarrhal jaundice. The etiology of hepatitis epidemica is still unknown. Diet does not play any rôle as a causative factor, but the infectious nature of the disease seems to be ascertained, and the conception that it is caused by a virus seems most likely. Epidemic hepatitis produces almost complete immunity. It is transmitted, most probably, by droplet infection and not by contamination of food or water. The contagious period may last for more than three weeks after the onset. The incubation period is believed to be from two to four weeks. In the early stages of the disease the temperature of the patient usually reaches 104 F. The prognosis is good. The mortality is from 0.2 to 0.4 per cent, with the deaths occurring chiefly in young infants. The value of the usual treatment (rest in bed, carbohydrates, insulin) is doubtful.

HEYMANN, Cleveland.

Successful Treatment of Bang's Disease with Prontosil (a Derivative of Sulfanilamide). W. Berger and H. Schnetz, Med. Klin. **33**:594 (April 30) 1937.

After five weeks of unsuccessful treatment with neoarsphenamine, a patient with Bang's disease made a permanent recovery following treatment with two derivatives of sulfanilamide, prontosil tablets (the hydrochloride of 4-sulfamido-2,′ 4′-diaminoazobenzene) administered orally and prontosil-soluble (the disodium salt of 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3,′ 6′-disulfonic acid) injected intramuscularly.

Siemsen, Chicago.

Epidemic Benign Icterus in Children. Popovici-Lupa and V. Petrescu-Coman, Monatschr. f. Kinderh. **70**:57 (April) 1937.

An epidemic of benign icterus affecting eighteen boys and fifteen girls is reported. Twenty of the patients were between the ages of 2 and 7 years and eleven were over 7. The disease started with gastro-intestinal symptoms, including vomiting, colic and diarrhea. There was malaise but rarely sore throat. Fever occurred at the beginning, and jaundice became evident on the fourth or fifth day. The liver was always enlarged and tender, and the spleen was usually palpable. The children all recovered. The etiology of the condition is unknown.

Gerstley, Chicago.

Studies on the Control of Fecal-Borne Diseases in North China: II. The Distribution of Ascaris Lumbricoides Infestations in a Rural Population. Gerald F. Winfield, Chinese M. J. **51**:502 (April) 1937.

This is the second contribution on the control of fecal-borne diseases in North China. In a third paper, which is yet to be published, the study of the epidemiology of Ascaris lumbricoides will be continued. The survey included the examination of 1,190 persons, 81 per cent of whom had ascariasis, the egg count averaging 14,000 per cubic centimeter. The counts for children were a little more than twice as great as those for adults. The habits of the people would tend toward the spread of ascariasis, while the small rainfall in this region would reduce parasitism. The article contains tables giving the data from which conclusions were drawn.

Neff, Kansas City, Mo.

Ya Tan Tzu—A New Specific for Amebic Dysentery. H. L. Liu, Chinese M. J. **52**:89 (July) 1937.

For a year Liu has employed a new therapy which is not so expensive as those usually employed, such as emetine and emetine bismuth iodide. The new drug is a preparation of the seeds of the plant Brucea, especially Brucea javanica. When a 2 per cent infusion of the powdered seeds (which have been rendered oil free) is mixed with an amebic stool, the amebas die at once. Nineteen cases were studied. The patients were treated with the seeds, shells removed (from 20 to 50 constituting a full dose). One dose, whole or divided, was given each day. The remedy is simple, cheap, effective and nontoxic; it is probably the best treatment yet devised. Eighty per cent of the patients were benefited, the parasites being destroyed in a short time.

Neff, Kansas City, Mo.

A New Anthelmintic "Raigan" in Teniasis. Sai Ryo, J. Orient. Med. **26**:799 (April) 1937.

"Raigan" is a variety of fungus found growing in bamboo forests, its scientific name being Omphalia lapidescens. In the form of a dried powder, it has a pronounced effect as an anthelmintic in the treatment of infection with Taenia solium, Taenia saginata, Hymenolepis nana, Hymenolepis diminuta and Dipylidiuim caninum. The drug has a destructive effect on the tapeworm, the effect being more evident as the segments approach the head. Healing is considered complete when there is no evidence of regeneration in four months. The drug has been used in China for nearly two thousand years.

Kato, Chicago.

Chronic Infectious Diseases

A Summary of the Results of Group Tuberculin-Testing with P.P.D. (Purified Protein Derivative) in the United States. Final Report of the National Tuberculosis Association. J. S. Whitney and I. McCaffrey, Am. Rev. Tuberc. **35**:597 (May) 1937.

In this paper are summarized the results of 85,709 group tests made with first and second strength purified protein derivative on 56,688 persons throughout the United States. With use of a stable tuberculin and a standardized technic, it was felt that a more reliable index of the incidence of tuberculosis in the United States could be determined. The adjusted percentage of positive reactors among all persons tested was 47. There were fewer positive reactors proportionately among 6 year old children than at any other age. Following the sixth year of life the trend of infection was generally upward at an average rate of over 1 per cent for each year up to the age of 20. Adults of 20 years and over evidenced 34 per cent more tuberculous infection than boys and girls under 20 years of age.

Among persons reported to have contact with tuberculosis, the positive reactors numbered 54.2 per cent, as compared with 33.3 per cent among those without such a history.

The percentage of positive reactors among white people, adjusted for age, nativity and percentage, was but 1 per cent lower than for Negroes, although the nonadjusted rate for white people was 15 per cent lower. The trend of infection among Negroes increased with age up to 20 at a faster rate than the trend among white people. Nativity and parentage seemed to be significant factors in tuberculous infection among the white persons tested. Of native-born Americans of native parentage, 27.6 per cent evidenced tuberculous infection, as compared with 34 per cent native-born Americans of foreign stock and 61.2 per cent of foreign-born persons.

Eugene Smith, Ogden, Utah.

Protracted Haematogenous Tuberculosis with Predominant Involvement of the Heart. S. Cohen, Am. Rev. Tuberc. **35**:618 (May) 1937.

Two cases of this condition are reported by Cohen with detailed clinical and postmortem observations. In case 1 there was unusual caseous involvement of all the chambers except the left auricle. The pericardium was primarily involved, with secondary invasion of the myocardium. The great vessels of the heart were also affected. The endocardium of the right auricle was invaded.

In case 2 the pericardium was the site of fibrocaseous tuberculosis with myocardial involvement. The right auricle presented a caseous nodule embedded in the muscle layer.

Eugene Smith, Ogden, Utah.

Effects of Vitamin-D Deficiency on Experimental Tuberculosis in the Rabbit. M. Steiner, M. R. Greene and B. Kramer, Am. Rev. Tuberc. **35**:640 (May) 1937.

In this study of the influence of vitamins on the pathogenesis of tuberculosis it was found that the rachitic condition apparently did not cause a decrease in the weight or in the period of survival of tuberculous rabbits except in one group with minimal lesions. Infected rachitic rabbits showed no greater incidence of infection and no more severe tuberculosis than did the controls. In animals protected by primary inoculation the reaction to reinfection was the same whether the animals were rachitic or nonrachitic.

Eugene Smith, Ogden, Utah.

Effect of Irradiated Milk Compared with Vitamin-D Oils on Inhalation Tuberculosis of Guinea Pigs. W. Steenken Jr. and E. R. Baldwin, Am. Rev. Tuberc. **35**:656 (May) 1937.

For the purpose of comparing irradiated milk and oils containing vitamin D as factors in the nutrition of tuberculous patients, mass feeding experiments were made with guinea pigs suffering from inhalation tuberculosis. It was found that

the feeding of irradiated cream containing double strength vitamin D had no influence on the development and course of inhalation tuberculosis in adult guinea pigs. This was also found to be true of cod liver oil and tuna liver oil with the same dosage of vitamin D units. Tenfold doses of these oils were less well borne, and a third of the animals died before the end of ten weeks. The survivors gave evidence of toxemia, but showed smaller spleens and less caseation. They showed no calcification.

EUGENE SMITH, Ogden, Utah.

A NOTE ON THE EFFECT OF SYNTHETIC ASCORBIC ACID (VITAMIN C) ON THE GROWTH OF THE TUBERCLE BACILLUS. C. H. BOISSEVAIN and J. H. SPILLANE JR., Am. Rev. Tuberc. **35**:661 (May) 1937.

Synthetic cevitamic acid in a concentration of 0.001 per cent inhibits the growth of human tubercle bacilli in artificial mediums. However, the daily injection of fifty times the antiscorbutic dose of this substance does not protect guinea pigs from infection with human tubercle bacilli. EUGENE SMITH, Ogden, Utah.

STUDIES WITH BCG: I. THE PRESENT METHOD OF BCG CULTIVATION AND VACCINE PRODUCTION AS PRACTICED AT THE PASTEUR INSTITUTE AND THE TICE LABORATORIES. S. R. ROSENTHAL, Am. Rev. Tuberc. **35**:678 (May) 1937.

The method used in the culture of the bacillus of Calmette and Guérin at the Pasteur Institute has not heretofore been reported in the American literature. This Rosenthal, former assistant of Dr. Guérin, details in his paper. The procedure described is now used in the Tice Laboratory of the Municipal Tuberculosis Sanitarium, Chicago.

EUGENE SMITH, Ogden, Utah.

STUDIES WITH BCG: II. ATTEMPTS AT DISSOCIATION AND INCREASE OF VIRULENCE. S. R. ROSENTHAL, Am. Rev. Tuberc. **35**:685 (May) 1937.

The opponents of the Calmette-Guérin method of vaccination believe that the organism can regain virulence. These antagonists may be divided into three groups: (1) those who believe that BCG grown according to the methods of Calmette and Guérin may produce in animals a slowly progressive and at times fatal tuberculosis; (2) those who believe that the virulence of BCG can be enhanced by animal passage, and (3) those who believe that dissociation may occur as noted by the virulent S forms or that by special methods of culture an increase of virulence may be effected.

Repeating the more important experiments of the investigators whose findings he has summarized, Rosenthal was unable to confirm their conclusions as to the instability of BCG. Using BCG prepared by Guérin, he was unable to produce progressive tuberculosis in a large group of animals. Passage of BCG through a series of animals did not enhance its virulence. On the contrary, a decrease in virulence was the rule. Repeating the experiments of the critics who appear to have shown that dissociation may be brought about by various culture methods, using cultures from the Pasteur Institute, he found that such dissociation in the sense of an increase in virulence did not occur. The colonies changed morphologically but more or less transitorily, probably with arrest or acceleration of the growth of the organism.

EUGENE SMITH, Ogden, Utah.

EVIDENCE OF THE PROTECTIVE INFLUENCE OF ADRENAL HORMONES AGAINST TUBERCULOSIS IN GUINEA PIGS. F. M. POTTENGER JR. and J. E. POTTENGER, Endocrinology **21**:529 (July) 1937.

Because it has been shown that rats can be rendered susceptible to tuberculosis by adrenalectomy, and because administration of adrenal products to tuberculous patients has been found by the authors to have an apparently beneficial effect, a series of experiments was carried out on guinea-pigs.

Experiments are detailed which show that extracts of the adrenal cortex exert an inhibiting influence on tuberculous infection in guinea-pigs.

Three series of experiments are presented in which animals treated with an extract of adrenal cortex are compared with untreated controls and with animals treated with other substances, in respect to longevity and to the extent and nature of the disease found at autopsy.

Of twenty-four untreated animals inoculated with 100 ± 10 tubercle bacilli obtained from fresh human sputums and five animals inoculated but treated with insulin, all became infected.

Twelve (28 per cent) of forty-three inoculated animals which received an extract of adrenal cortex for periods varying from ten days to their entire life showed at autopsy no evidence of tuberculous infection. It was further found that infection, when present, differed from that in untreated animals in that it was milder and less extensive.

JACOBSEN, Buffalo.

A "RAPID" MICRO-HINTON AND CAPILLARY HINTON TEST FOR SYPHILIS WITH A DISCUSSION OF THE DETECTION OF SYPHILIS BY SEROLOGIC METHODS. J. A. V. DAVIES, J. Pediat. **10**:802 (June) 1937.

Davies has developed a micro-Hinton and a capillary Hinton flocculation test which employ small amounts of serum—0.2 cc. and 0.05 cc., respectively. The blood is obtained by puncture of the skin with a no. 11 Bard-Parker blade and collected either in a long Wright tube or in a capillary tube. Over 500 specimens have been examined by these methods, and the results of 464 of the tests were checked against the results of other tests and the clinical diagnoses. False negative reactions were rare, and only 5 false positive reactions occurred. These were associated with febrile illnesses, and in 4 of the 5 instances the reactions subsequently became negative. The final reading of the test, with either method being used, may be made in an hour, if necessary, without demonstrable loss in sensitivity. The importance of repeated blood tests in the neonatal period and in the first few months of life is stressed, and the advantage of using small quantities of blood serum is pointed out.

RAUH, Cincinnati.

FURTHER EVIDENCES OF ORAL BISMUTH ACTIONS. P. J. HANZLIK, A. L. LEHMAN and W. VAN WINKLE, J. Pharmacol. & Exper. Therap. **60**:111 (June) 1937.

These authors have previously shown that oral administration of a soluble bismuth salt was effective in preventing and curing experimental syphilis. The present note is a brief summary of the effective clinical prophylactic and curative action of sodium bismuthate soluble given by mouth.

PILCHER, Cleveland.

HEREDITARY SYPHILIS. F. H. CHURCH, M. Rec. **145**:499 (June 16) 1937.

Church states that heredosyphilis may be divided into three groups: (1) effects of syphilis on heredity, or tribal syphilis; (2) constitutional syphilis, or familial syphilis; (3) congenital syphilis, or prenatal syphilis. He then discusses each group, also the pathology of constitutional syphilis and the roentgenologic study of the bones in syphilis.

WILLIAMSON, New Orleans.

COMPARATIVE STUDY OF TUBERCULIN REACTIONS AND RADIOLOGICAL FINDINGS. O. SCHEEL, Lancet **1**:922 (April 17) 1937.

The majority of the patients used in this study came from the university clinic for patients with tuberculosis at Oslo. The 1,697 students studied were without previous history of tuberculous disease or of BCG vaccination. They were studied from the angle of their reactions to tuberculin and roentgenologic findings.

Scheel emphasizes that with the Pirquet technic he always finds a higher tuberculous morbidity among those whose Pirquet reactions are negative than among those who show positive Pirquet reactions when both groups are exposed to infection; 851 students had negative and 846 positive reactions to tuberculin.

From the roentgenologic point of view the patients were divided into three groups: 1. Those with changes in the pleura, usually diaphragmatic adhesions,

sometimes thickening over the apex, but without changes in the lung or the hilus. 2. Those with shadows in the lung fields and in some cases changes in the pleura, but without calcification. 3. Those with deposits of calcium in the lung tissue or the glands; in these there may be, in addition, pleural and pulmonary shadows.

The purely pleural changes appear with approximately equal frequency among those with negative and those with positive reactions to tuberculin (from 0 to 6.5 per cent).

The pure pulmonary shadows without calcifications, presumably corresponding to deposits of fibrous tissue, are distinctly more frequent among those with positive (from 0 to 6.9 per cent) than among those with negative (from 0 to 1.6 per cent) reactions.

Calcified foci occur, though rarely, among the patients with definitely negative reactions to tuberculin (0.7 per cent), whereas they are not infrequent in the patients with positive reactions (from 12.2 to 16.2 per cent).

LANGMANN, New York.

TUBERCULOUS GLANDS OF THE NECK IN CHILDREN—RESULTS OF SURGICAL TREATMENT. L. BARRINGTON-WARD, Lancet **1**:980 (April 24) 1937.

This report from the Hospital for Sick Children, Great Ormond Street, gives the results in 95 children who could be traced. Ninety-four were living; one had died of mastoiditis and streptococcic meningitis. Eleven patients had slightly enlarged glands in a different part of the neck. The average stay in the hospital for these children treated by dissection was twenty-two days. Only three of eighty-nine patients had a discharge from the wound after operation. In one case the discharge persisted for six months.

The author emphasizes that in many cases the glandular enlargement will recede and disappear under general supportive treatment.

If dissection is undertaken, all the glands in the affected area "can and should be dissected out."

LANGMANN, New York.

ANTITUBERCULOSIS WORK IN EGYPT. M. S. ABAZA BEY, J. Egyptian M. A. **20**:241 (June) 1937.

Abaza Bey presents a plea for better coordination of antituberculosis work in Egypt. He quotes the findings in an epidemiologic study in cities such as Cairo and Alexandria showing the percentage of positive reactions to old tuberculin in a dilution of 1:5,000 to be 96 in adults and about 60 in children below 15 years of age. He states that 2,801 cases were reported in one year from six dispensaries treating patients who present themselves voluntarily. Medical practitioners at large take little advantage of expert opinion, refusing to recognize the rôle of specialists. There is at present one sanatorium, at Helwan, with a capacity of 400 beds. There are a number of dispensaries satisfactorily equipped. The patients in whom tuberculosis is diagnosed here are divided into two groups. Those judged to be of the institutional type are put on the waiting list for the one sanatorium. Those judged to have the disease too advanced are supervised in their homes. The housing conditions are poor. There are severe overcrowding and much ignorance of the rudiments of hygiene. There is no organization for the care of patients after their discharge from the hospital, and no means are available to help such patients find suitable occupations or to care for their families while they are hospitalized.

Though the government intends to increase the number of dispensaries and sanatoriums, the author feels a more effective and cheaper manner of approach to the problem would be through the establishment of village colonies.

There is only a loose association between the medical officer of health, the school doctors and the tuberculosis officer, and the author feels these should be coordinated under one head.

In a climate as equitable as that of Egypt he notes a deplorable lack of open air schools.

MULHERIN, Augusta, Ga.

A Clinico-Anatomic Contribution to the Study of Congenital Pulmonary Syphilis (White Pneumonia). M. Radici, Riv. di clin. pediat. **35**:481 (June) 1937.

The patient, a 2 year old boy, for about four months before death had fever, dyspnea, cyanosis and cough; he was also undernourished, anemic and rachitic. At necropsy the lungs were found to have lesions typical of the white pneumonia of syphilis.

Higgins, Boston.

Froin's Syndrome in a Patient with Tuberculous Meningo-Encephalitis. R. Galeno and A. Fialho, J. de pediat., Rio de Janeiro **4**:265 (July) 1937.

A child 2 years of age showed a typical Froin syndrome (spinal fluid xanthochromic, with massive coagulation). Autopsy revealed a tuberculous infiltration of the brain and meninges. Interesting photomicrographs are shown.

Sanford, Chicago.

Tuberculosis Incidence Among Chinese Children. A. V. Scott, Chinese M. J. **51**:851 (June) 1937.

The object of the investigation reported was to learn more about the age when children in China are acquiring tuberculous infections. The survey permits comparison of rural school children with children of similar ages in the city. The routine test was an intradermal injection of 0.1 mg. of old tuberculin. The incidence of positive reactors was as follows:

	Urban	Rural
Males	45.9%	44.68%
Females	49.6%	52.5%

The percentage for Chinese girls is definitely higher because they stay at home more commonly, and in China tuberculosis spreads chiefly in the home.

Enlarged mediastinal and peribronchial shadows are the most common roentgen findings in childhood. Of the children showing positive skin reactions 215 had x-ray pictures showing tuberculous involvements, and these were usually most frequent at the age of from 7 to 10 years.

Neff, Kansas City, Mo.

Perforation of a Tuberculous Mesenteric Gland. W. de Wyn, Nederl. tijdschr. v. geneesk. **81**:2728 (June 12) 1937.

De Wyn reports a case of tuberculosis of the mesenteric glands with perforation of one of the glands in a boy of 16 years. The treatment consisted in resection of the glandular mass with the corresponding sector of mesentery and small intestine. After five months of heliotherapy and a diet rich in vitamins, complete recovery ensued.

van Creveld, Amsterdam, Netherlands.

Diseases of Blood, Heart and Blood Vessels and Spleen

Toxicity and Effect of Congo Red upon Blood Coagulation. I. Taliaferro and H. B. Haag, Am. J. M. Sc. **193**:626 (May) 1937.

Congo red has been employed, among other clinical tests, for estimating the functional state of the reticulo-endothelial system and for determining amyloid disease. It has also been used empirically in treating pernicious anemia. The dye is reported to be advantageous as a hemostatic agent in cases of pulmonary tuberculosis, uterine bleeding and extraction of teeth in persons with hemophilia or purpura haemorrhagica.

Ten patients were given intravenous injections of from 10 to 15 cc. of a 1 per cent solution of congo red. Tests made on blood from their veins showed in the majority a definite decrease in coagulation time following administration of the dye.

Henske, Omaha.

DIETARY DEFICIENCY AS A CAUSE OF MACROCYTIC ANEMIA. J. GROEN and I. SNAPPER, Am. J. M. Sc. **193**:633 (May) 1937.

A clinical picture closely resembling that of pernicious anemia was observed in two cases in which the histories revealed a prolonged and pronounced dietary deficiency. Subnormal amounts of free hydrochloric acid were found in the gastric juice. Further features included an improvement of the gastric secretion by the dietary treatment and a flat type of blood sugar curve, indicating poor intestinal absorption, when the condition was severe.

It is suggested that the macrocytic anemia was due to a deficiency of Castle's extrinsic, rather than intrinsic, factor. Anemia of this type which appears analogous to the tropical macrocytic anemia reported by Wills is probably more frequent than commonly believed. Many cases of so-called pernicious anemia with free hydrochloric acid in the stomach appear to belong to this group.

HENSKE, Omaha.

THE LEUKOPENIC INDEX WITH REFERENCE TO NORMAL WHITE BLOOD CELL VARIATIONS. M. ZELLER, Am. J. M. Sc. **193**:652 (May) 1937.

Serial white blood cell counts taken under resting and fasting conditions are consistently uniform, with variations not exceeding 750 cells. The larger variations are infrequent, the counts for the most part being within from 200 to 300 cells of one another. The influence of mild and violent exercise is noted by a definite white cell increase, with a return to the preexercise period in thirty minutes. Heavy and light meals evoke white cell responses increasing in proportion to the quantity of food ingested and sustained in gradually decreasing numbers for as long as three hours. Previously reported work on white blood cell responses used as a criterion for questioning leukopenic index studies cannot be accepted as a basis for evaluation, since the conditions of the experiments were dissimilar.

HENSKE, Omaha.

PERNICIOUS ANEMIA IN AN INFANT. F. S. LANGMEAD and I. DONIACH, Lancet **1**:1048 (May 1) 1937.

A case of pernicious anemia in a 13 month old boy fulfilled the criteria of Parsons and Hawksley for this diagnosis in that the anemia was hyperchromic with a megalocytosis of 6.8 per cent, the icteric index was 17.6 units, the red cells showed considerable poikilocytosis, no free hydrochloric acid was secreted in response to histamine, and there was a reticulocyte response of 19 per cent to an extract of liver when his red cell count was 2,000,000. He was treated with liver and iron and discharged from the hospital clinically well and with a normal blood picture.

NOTE.—Dr. W. Carey Smallwood (Children's Hospital, Birmingham) suggests in the *Lancet*, May 8, 1937, that this is a case of subacute hemolytic anemia rather than pernicious anemia.

LANGMANN, New York.

FAMILIAL HEMOLYTIC JAUNDICE. U. VIGNOLO and F. SEMAH, Riv. di clin. pediat. **35**:385 (May) 1937.

The case of an 8 year old girl with familial hemolytic jaundice is described. The father had the same disease in a much milder form. A satisfactory cure followed removal of the spleen, which weighed 700 Gm.; not only was the blood disturbance relieved, but the child improved nutritionally.

HIGGINS, Boston.

EFFECT OF ADMINISTRATION OF VARIOUS COAGULANTS, OF VITAMIN C AND OF LIVER EXTRACT ON THE FIBRINOGEN AND OTHER COAGULATING FACTORS IN THE BLOOD OF THE CHILD. A. FARIOLI and E. MEDDA, Riv. di clin. pediat. **35**:405 (May) 1937.

Observations were made with three commercial products: trombocitina, coagulenо and zimema.

Trombocitina is a tissue extract. In vitro it increased the blood coagulation time. When it was given to children, there was an increase in the fibrinogen of the blood, which was slow in appearing but persisted over a considerable time.

Coaguleno is made from blood platelets. In vitro it increased the coagulation time. In vivo it did not increase the fibrinogen of the blood, but it slightly accelerated the coagulation time.

Zimema is a product containing a fibro-enzyme, held in emulsion by physiologic serum. In vitro it acted to speed the coagulation time. In vivo it caused the fibrinogen of the blood to show an immediate and persistent increase.

Cevitamic acid did not affect the coagulation time of blood in vitro but did increase the fibrinogen content of blood when it was fed to children.

Liver extract in vitro had no effect on the coagulation time, but when given to children it caused increase in the amount of fibrinogen in the blood.

HIGGINS, Boston.

THE CLINICAL TEST OF THE BLOOD'S BACTERICIDAL POWER. H. FAJERMAN, Nederl. tijdschr. v. geneesk. **81**:2335 (May 22) 1937.

The best temperature for putting up blood for tests of bactericidal power is ordinary room temperature, or about 18 C. (64.4 F.). The lapse of time between taking the blood sample and carrying out the test should not exceed three hours. Addition of sodium citrate in a concentration of 2:1,000, 1:1,000 or even 0.5:1,000 markedly impairs the bactericidal power of the blood; this change is mainly brought about by an action of the citrate on the serum. Impairment of bactericidal power can likewise be observed after intravenous administration of large doses of sodium citrate. Therefore a prophylactic injection of a soluble calcium salt is advisable in the practice of immunotransfusion with citrated blood.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Nose, Throat and Ear

CHRONIC SINUSITIS WITH EARLY BRONCHIECTASIS. S. CAMPBELL, Proc. Roy. Soc. Med. **30**:708 (April) 1937.

A case in a boy of 11 years is reported. At the age of 5 years he had an attack of pneumonia; at 6 years, diphtheria and pneumonia, and at 7 years, whooping cough and measles. Tonsillectomy and bilateral antrostomy were performed when he was 8 years old. After that he had repeated attacks of bronchitis and for the last two years had persistently brought up large quantities of sputum the first thing in the morning and again in the evening. He became short of breath on exertion. On admission to the hospital coarse râles were heard at the bases of the lungs and the fingers were clubbed. With postural drainage 50 cc. of sputum was produced daily. X-ray films showed increased markings at the bases of both lungs. Iodized poppy-seed oil 40 per cent showed slight dilatation of the bronchi at the base of the right lung. Both maxillary sinuses were opaque The report is accompanied by reproductions of roentgenograms of the chest taken following the introduction of iodized oil and of the skull.

WILLIAMSON, New Orleans.

PSEUDOMEMBRANOUS RHINITIS. G. SALVADORI, Méd. inf. **8**:141 (May) 1937.

Pseudomembranous rhinitis may be divided into two groups: (1) diphtheritic and (2) pyogenic (diplococcic, streptococcic or staphylococcic). Salvadori reports three cases of pseudomembranous rhinitis in none of which diphtheria organisms were found. Two of the children responded well to local treatment with strong protein silver. The third patient, who showed a higher fever and more marked cervical adenitis and appeared sicker, did not respond to local treatment but rapidly got well following the giving of diphtheria antitoxin.

HIGGINS, Boston.

Diseases of the Gastro-Intestinal Tract, Liver and Peritoneum

ABNORMALITIES OF THE ROTATION OF THE MIDGUT: A REPORT OF FOUR CASES. G. DANELIUS, Am. J. Digest. Dis. & Nutrition **4**:231 (June) 1937.

The embryology of the midgut in relation to the foregut and hindgut is thoroughly reviewed. The anomalies are then listed as (1) nonrotation, (2) reversed rotation and (3) malrotation. The patients presenting these anomalies are divided into four groups as follows:

Group 1. In this group the patients are symptom free, and the anomaly is found accidentally during an abdominal operation or as a true appendix of the left side or as a surprise at necropsy.

Group 2. This group comprises patients with vague gastro-intestinal symptoms, such as discomfort, moderate pain, a feeling of vague pressure, belching and sometimes mild constipation. It is impossible to make a diagnosis clinically, but the malformation can be seen on roentgen examination.

Group 3. These patients have acute intestinal obstruction and are usually operated on, with complete disappearance of all symptoms.

Group 4. In these infants high intestinal (duodenal) obstruction in abnormal rotation becomes evident around the third to eighth day of life. The infants become acutely ill and vomit from one half to one hour after feeding. Owing to the location of the stenosis below the papilla of Vater, the stomach contents are bile stained, and the stools become colorless. The upper part of the abdomen is distended; the lower part is scaphoid. The patient becomes dehydrated. Clinically, differentiation of this condition from congenital atresia of the intestine is impossible. In pyloric stenosis the gastric contents are colorless.

The majority of these infants show adhesions between the lower part of the duodenum and the last loop of ileum, due to malrotation. Occasionally, nonrotation or reversed rotation is found. Operations such as gastro-enterostomy offer the only hope of saving the patient.

A roentgenologic technic adequate to demonstrate the condition is described.

A report of four observations is given, one being that of a boy who presented typical signs of a nonrotated midgut.

MORRISON, Savannah, Ga.

HOW DO BULKY FOODS RELIEVE CONSTIPATION? W. C. ALVAREZ, Am. J. Digest. Dis. & Nutrition **4**:240 (June) 1937.

This is an editorial by Alvarez in which no attempt is made to answer the question.

Mineral oil, agar, vegetable roughage and fruits are discussed, with the catabolism of each as it passes through the gastro-intestinal tract.

This editorial appears mainly as a stimulus to experimental work on this unknown subject.

MORRISON, Savannah, Ga.

PRIMARY TUBERCULOUS APPENDICITIS AND APPENDICITIS COMPLICATING PULMONARY TUBERCULOSIS. E. T. THIEME, Am. J. M. Sc. **193**:700 (May) 1937.

Seven cases of so-called primary tuberculous appendicitis are reported. In two of the cases tuberculosis elsewhere was found later. The history and physical findings in these seven cases were essentially the same as in cases of pyogenic appendicitis, and the diagnosis was not made preoperatively. The prognosis was uniformly good.

Twenty cases of pulmonary tuberculosis in which operations were performed for appendicitis were reviewed; the lesion was acute in thirteen and recurrent in seven. Of the twenty patients, six had tuberculous appendicitis; five of them were doing poorly preoperatively from the pulmonary standpoint. Of the six, five are dead, and the sixth is critically ill. The extremely poor prognosis of tuberculous appendicitis in uncontrolled advanced pulmonary disease is evident. The fourteen cases of pyogenic appendicitis occurred in patients who were doing well from the

standpoint of their pulmonary tuberculosis. Their subsequent course has been such as to lead the author to believe that their appendicitis was unrelated to their tuberculosis and did not affect the course of that disease. HENSKE, Omaha.

FURTHER STUDIES ON BACTERIUM NECROPHORUM ISOLATED FROM CASES OF CHRONIC ULCERATIVE COLITIS. G. M. DACK, L. R. DRAGSTEDT and T. E. HEINZ, J. Infect. Dis. **60**:335 (May-June) 1937.

Bacterium necrophorum has been commonly found associated with ulceration of the colon in man and monkeys. In chronic ulcerative colitis in man it has been found in enormous numbers in the lesions as shown by cultures from material obtained at proctoscopic examination. It outnumbers other organisms in isolated severely diseased colons of patients on whom ileostomies have been performed. It has not been recovered after healing of the bowel. It appears to be present in the bowel, since it readily appears when necrotic lesions develop in the colon, regardless of the inciting cause, i. e., bacillary dysentery, trauma or other disturbances.

Bacterium necrophorum does not appear to be a clearly defined bacterial species and has received many different names. It is similar, if not identical, to what is called in the literature Bacillus funduliformis. TOOMEY, Cleveland.

CONGENITAL OBSTRUCTION OF THE ALIMENTARY TRACT. H. A. REISMAN, J. Pediat. **10**:622 (May) 1937.

Eight cases of congenital obstruction of the alimentary tract are reported. Seven occurred in males. In two cases esophageal atresia was present; in one case, partial atresia of the esophagus with narrowing of the lower third; in one, partial atresia of the distal end of the duodenum. The sole operative recovery occurred in a case of congenital obstruction of the ileum. Two cases of obstruction of the colon, one in which it was complete and one in which it was incomplete, are included in the report also a case of obstruction of the jejunum due to volvulus, with symptoms appearing immediately after birth.

Duodenal obstruction is differentiated from pyloric stenosis by the presence of bile in the vomitus and by the results of roentgen examination after a barium sulfate meal. Examination of the meconium will differentiate a complete from an incomplete obstruction of the intestines or absence of obstruction. In complete obstruction, particularly if the obstruction is high, meconium may be passed, but lanugo hairs and vernix caseosa will not be present. The vernix caseosa has a distinct microscopic appearance in that sheets of cornified epithelial cells are found which are characteristic and cannot be mistaken for anything else.

RAUH, Cincinnati.

RECURRENT VOMITING IN CHILDREN: ITS ETIOLOGY AND TREATMENT. C. H. SMITH, J. Pediat. **10**:719 (June) 1937.

This is a review of sixty-five cases of recurrent and cyclic vomiting seen by Smith in private and hospital practice during the past twenty years. The condition is seen more often in private practice than in hospital or outpatient work. A description of the attacks is given, with a detailed discussion of the causes. Every kind of disturbing factor, such as the onset of an acute illness, unusual nervous excitement, an accident or an exciting movie, may precipitate an attack. Ketosis does not precipitate an attack but merely accompanies it. The attacks occur, as a rule, in neuropathic children, the members of whose families are usually high strung and of more than average intelligence. Also in these families there is a tendency to migraine, cyclic vomiting and prematurely gray hair, especially on the maternal side. Family trees are presented to illustrate the association of migraine, cyclic vomiting and premature grayness. The author believes that recurrent vomiting is a childhood equivalent for migraine and gives the following reasons: 1. There is the family association. 2. A number of the children with cyclic vomiting grow up to have migraine in adolescence or young adult life.

3. Some of the children become gray before they are 30. 4. In both conditions treatment with sedatives or analgesics usually stops an attack. In treatment the important step is to stop the vomiting with sedatives. Treatment of the ketosis alone will not stop the vomiting, and the ketosis needs to be treated only in those patients who have vomited for several days.

RAUH, Cincinnati.

A CASE OF VON GIERKE'S DISEASE WITH MARKED LIPEMIA. P. HOGG and J. B. SIDBURY, J. Pediat. **10**:798 (June) 1937.

A 16 month old infant suffering from von Gierke's disease showed hepatomegaly, hypoglycemia, acetonuria and aglycogenolysis. In addition, a marked lipemia was present, 2.770 Gm. per hundred cubic centimeters. The authors suggest that the faulty carbohydrate metabolism accounts for the lipemia.

RAUH, Cincinnati.

LYMPHATIC CYST OF THE MESENTERY AND VOLVULUS IN A CHILD. R. C. JEWESBURY, Lancet **1**:1170 (May 15) 1937.

A girl 5 years and 8 months of age first complained of abdominal pain at the age of 2 years. Between that time and her admission to the hospital she had had several severe and numerous minor attacks. On examination she presented an "abdominal facies" and a distended abdomen, free from pain or tenderness. A laparotomy was done, a volvulus of the small intestine was found, and a cyst in the pelvis containing from 15 to 16 ounces (443.5 to 473 cc.) of thin milklike fluid. The child died four hours after operation. At postmortem examination a mark encircling the bowel and obviously due to a strangling construction was found ½ inch (1.27 cm.) above the ileocecal valve.

LANGMANN, New York.

CLINICAL FEATURES OF INTESTINAL INFANTILISM. G. LÉVY and E. LANDA, Arch. de méd. d. enf. **40**:207 (April) 1937.

Under different names, such as "Herter-Huebner syndrome," "pancreatic infantilism," "acholia" and "celiac disease," this chronic digestive disorder has been recognized since its first description by Gee in 1888. It is found in children beyond the first year of life but is said to be extremely rare in certain countries, particularly France, Italy and Hungary.

The chief characteristics of intestinal infantilism are: (1) marked arrest of growth; (2) enormous spherical distention of the abdomen, with general atrophy and pallor; (3) abundant fetid stools, containing much fat; (4) hypotonia and muscular weakness with resulting loss of activity; (5) severe secondary anemia, and (6) enlarged colon, displaced to the right. The fundamental pathognomonic symptom in these cases is the typical stool, with frequent relapses in the so-called dyspepsia of fermentation (Schmidt). MacCredon expressed the belief that the pathogenesis rests not so much on decrease in absorption as on insufficiency of the primitive impulse to grow.

Hydrolability is another striking feature, the infant often losing as much as a tenth of its body weight in twenty-four hours through a badly selected ration or following a slight infection. Authorities are as much at variance as ever respecting the etiology of this strange disease, but there is a measure of agreement as to treatment, which follows the plan adopted in most American clinics. The authors report four cases in full.

AMESSE, Denver.

GUANIDINEMIA IN ALIMENTARY INTOXICATION OF INFANTS. F. RUBINI, Lattante **8**:297 (May) 1937.

In the blood of eleven of fifteen infants with intestinal intoxication Rubini found an abnormally large amount of guanidine. Since the action of calcium is antagonistic to that of guanidine, calcium therapy seems indicated as a routine procedure in intestinal intoxication.

HIGGINS, Boston.

PYLORIC STENOSIS IN THE INFANT. C. COCCHI, Lattante **8**:317 (May) 1937.

Three cases of pyloric stenosis in infants are reported. One child was treated surgically (Rammstedt operation) and got well. A second was treated medically and also got well. The third developed bronchopneumonia and died; an autopsy was performed.

Cocchi calls attention to the anatomy and physiology of the pylorus. There is a pyloric sphincter, which opens and closes to let the chyme pass into the duodenum. On the stomach side of the sphincter is the pyloric antrum, which is a tube or pouch containing chyme, which at a given peristaltic contraction is pushed through the open sphincter into the duodenum. Between the pyloric antrum and the stomach is a valve which closes during peristalsis of the antrum and opens with constriction at the sphincter. Hypertrophic stenosis of the pylorus represents stenosis not at the pyloric sphincter but of the entire pyloric antrum. There is hypertrophy of the smooth muscle of the antrum, also some hyperplasia of the submucous tissue and mucous membrane. The stomach, in endeavoring by peristalsis to push along the chyme, must push against a constricted antrum. In the Rammstedt operation it is the hypertrophied muscles of the antrum of the pylorus which are cut rather than the muscles of the pyloric sphincter; in fact, if the muscles of the pyloric sphincter are cut one is almost certain to enter the duodenum.

HIGGINS, Boston.

THE PRESENT STATUS OF OPERATIVE TREATMENT OF PYLORIC STENOSIS IN INFANTS. M. KIRSCHNER, Med. Klin. **33**:785 (June 11) 1937.

Mortality statistics definitely favor surgical treatment of pyloric stenosis, and surgical treatment offers the advantage of rapid recovery. Unless the patient improves decidedly in a short time on medical management, surgical intervention is indicated. Delay increases the operative risk and predisposes to intercurrent infections. Kirschner usese a modified Rammstedt technic which aims at simplicity and dispatch.

SIEMSEN, Chicago.

PATHOGENESIS OF GLYCOGEN DISEASE. F. LINNEWEH, Monatschr. f. Kinderh. **70**:238 (May) 1937.

This is an unnecessarily verbose article in which it is maintained that underlying the pathogenesis of von Gierke's disease there is a state of hyperinsulinism. This is expressed in carbohydrate hunger, hypoglycemia, a tendency toward depositions of fat and increased synthesis of sugar. The last is demonstrated in experiments with dioxyacetone.

GERSTLEY, Chicago.

PRIMARY LIVER CANCER IN A CHILD. T. OHTA and I. NISHIUCHI, J. Orient. Med. **26**:983 (May) 1937.

A boy 5 years and 1 month old came to the attention of the authors because of a gradually enlarging abdomen. Physical examination revealed a pale undernourished child in whom the only positive finding was enlargement of the liver, its lower border reaching 8 cm. below the costal margin. Exploratory laparotomy disclosed definite masses of a tumor in the substance of the liver, with some fibrous adhesions of the organ to the surrounding serous surfaces. A small specimen of tissue was removed from one of these masses. Microscopically the sections of this material revealed small round cells with hyperchromatic nuclei, the cells being arranged in rosettes of varying sizes, resembling transverse sections of small tubules. These groups of pathologic cells were surrounded by strands of connective tissue, and in the larger rosettes necrotic centers were numerous. The subsequent course of the condition was not followed.

KATO, Chicago.

INTRAPERITONEAL BLOOD TRANSFUSION. H. P. J. KOENEN and J. M. M. VONK, Maandschr. v. kindergeneesk. **6**:320 (May) 1937.

The authors recommend the intraperitoneal blood transfusion and base their opinion on experience in fifty transfusions in very young children.

VAN CREVELD, Amsterdam, Netherlands.

Nervous Diseases

TREATMENT OF HEMOLYTIC STREPTOCOCCIC MENINGITIS WITH PARA-AMINO-BENZENE-SULFONAMIDE: REPORT OF A CASE WITH RECOVERY. J. G. ARNOLD, Ann. Int. Med. **10**:1198 (Feb.) 1937.

The patient was a white woman aged 28. A complete history of her case with details of the treatment are included in the report.

Twenty cubic centimeters of an 0.8 per cent solution of para-aminobenzene-sulfonamide (sulfanilamide) in physiologic solution of sodium chloride was injected intraspinally. This dose was given at intervals until four successive cultures of spinal fluid were negative. In addition, this substance was given orally in the form of tablets for eleven days following the last positive culture of spinal fluid.

The drug is considered to be relatively nontoxic. Sulfhemoglobinemia and acidosis may occasionally be encountered following its use.

READING, Galveston, Texas.

SERUM DISEASE OF THE NERVOUS SYSTEM. W. M. KRAUS and L. B. CHANEY, Arch. Neurol. & Psychiat. **37**:1035 (May) 1937.

This article summarizes the serum diseases of the central nervous system. The authors feel that the cause of these conditions is a foreign protein and not a specific antitoxin. Identical pictures result from the administration of serums used to prevent tetanus, diphtheria, scarlet fever, gangrene infection and pneumococcic, gonococcic, streptococcic and meningococcic infections and also from the administration of horse serum.

The authors summarize pathologic reports. The clinical picture usually presents itself after about seven days. There are as a rule high fever, urticaria, severe neuralgia, headache, nausea and vomiting—evidence of meningeal irritation. After the initial onset, the picture varies greatly. There may be cerebral, spinal, radicular or neural symptoms. Isolated nerve groups or single cranial nerves may be affected.

The prognosis is generally good, but recovery may not take place for months. Atropine, epinephrine, dehydration and spinal puncture are indicated.

BEVERLY, Chicago.

ENCEPHALOGRAPHY WITH ANESTHETIC CASES. R. B. AIRD, Arch. Surg. **34**:853 (May) 1937.

After experimentation by injection of various gases into dogs, encephalography with nitrous oxide and ethylene was attempted in man. In both children and adults the sedative action of the anesthetic gases tended to lessen the severity of the immediate reaction and materially assisted in making the procedure easier and the roentgenologic results more satisfactory. The rapid absorption of the anesthetic gases resulted in shortening the reaction after encephalography. The period of headache, nausea and malaise was reduced from about three days to one day. In children the sedative effect of the anesthetic gases insured a satisfactory procedure throughout and necessitated only an initial induction of anesthesia. Of the two anesthetic gases, ethylene is the more practical. The absorption of nitrous oxide is so rapid that good roentgenographic results cannot be insured. Aird feels that the use of nitrous oxide or ethylene is far superior to the use of air.

KAISER, Rochester, N. Y.

INTRACRANIAL DERMOID. N. H. GLADSTONE, J. Indiana M. A. **30**:282 (June) 1937.

Gladstone describes an intracranial dermoid in the region of the cerebellum, which communicated with the subcutaneous tissues of the scalp in the occipital region, where three incisions at intervals yielded purulent material. The child, aged 1 year, showed projectile vomiting. Later, convulsions and hydrocephalus ensued. Autopsy showed a cerebellar abscess due to degeneration of the dermoid and a congenital hydrocephalus.

MILLER, South Bend, Ind.

PERIPHERAL NEURITIS DUE TO LEAD. J. E. BROWN JR. and E. E. SMITH, J. Pediat. **10**:656 (May) 1937.

Uncomplicated peripheral neuritis with sensory changes due to lead poisoning is uncommon in childhood. Such a case was observed by Brown and Smith in a 3 year old white child. There were marked foot drop and wrist drop, with atrophy of the thenar eminences and diminution of sensation over the involved extremities. The literature is reviewed, and a brief discussion of the syndrome is given.

RAUH, Cincinnati.

NONHEMOLYTIC STREPTOCOCCUS MENINGITIS. R. G. HODGES, J. Pediat. **10**:666 (May) 1937.

Since 1919 only two cases of cerebrospinal meningitis due to a nonhemolytic streptococcus have been reported. This is a report of a fatal case in a 9 year old white girl, who was also suffering from congenital heart disease—the tetralogy of Fallot.

RAUH, Cincinnati.

ACUTE LYMPHOCYTIC MENINGITIS. W. HUGHES, Brit. M. J. **1**:1063 (May 22) 1937.

Two cases of this condition occurring in the tropics are reported. The author points out the difficulty of making a diagnosis, especially in the presence of a number of other conditions which are common to the tropics and which exhibit symptoms referable to the central nervous system.

ROYSTER, University, Va.

TUMOURS OF THE BASE OF THE BRAIN: THEIR RELATION TO PATHOLOGICAL SLEEP AND OTHER CHANGES IN THE CONSCIOUS STATE. L. B. COX, M. J. Australia **1**:742 (May 15) 1937.

The purpose of Cox' paper is to show that lesions of the brain other than those of the cortex may cause profound alterations in the conscious state as shown by conduct. He reports six cases of tumor of the brain involving the midbrain, hypothalamic region and thalamus, in each of which the invasion was accompanied by certain changes in the conscious state, such as drowsiness and hypersomnia, trancelike conditions, periods of apathy, catatonic states, alterations in disposition, disorientation for time and place, marked loss of memory and mental excitement.

GONCE, Madison, Wis.

PSYCHIC DISTURBANCES IN SYDENHAM'S CHOREA. G. NERI, Méd. inf. **8**:161 (June) 1937.

Neri has reviewed eighty-eight cases of chorea, seventy-two in patients attending the pediatric clinic of Bologna between 1925 and 1935 and sixteen in private patients. Fifty-one patients were girls, and thirty-seven boys. Sixty-five were cured; twenty-one, improved; one, unimproved, and one, dead (of bronchopneumonia). There was preceding rheumatic fever in thirty-four cases, endocarditis in twenty-three of them. In twenty-seven cases endocarditis had developed without any history of preceding rheumatic fever; in eight of these there

was a family history of rheumatic fever. There were no indications of rheumatic fever or of endocarditis in twenty-seven cases. There was a family history of syphilis in five cases, but the Wassermann reactions of the children were negative. In six cases there was a neuropathic family history. Nineteen of the patients had had recurrences of chorea. The mothers of two of the patients had had chorea.

Some psychic disturbances were present in between 50 and 60 per cent of the patients. Three showed marked neuromental instability and had hallucinations; these patients had had neuropathic tendencies before the onset of their chorea. The mental age of the patients with chorea was essentially normal. The reasoning and judgment were not appreciably altered. The memory was good. The disposition was usually good, although subject occasionally to emotional upsets. Attention was distinctly defective in that the patients could not concentrate on a subject for any length of time. The neuromental stability was definitely diminished, and disturbance of this was the most frequent psychic manifestation; the children passed easily from laughing to crying and were easily upset by things they saw; tact was required to maintain their confidence; their temperament was usually composed but very subject to outside influences.

HIGGINS, Boston.

PATHOGENESIS OF CEREBROSPINAL MENINGITIS. C. DOPTER, Paris méd. **1**:469 (May 29) 1937.

This is a discussion of the mode of entry of the meningococcus producing meningitis. There are two theories: First, it is thought that there is a direct entrance through the mucosa of the respiratory tract and the tissues related to the pituitary stalk. Second, it is supposed that an intermediary septicemia is present previous to the invasion of the meninges. No particular conclusions are drawn except that the original penetration is through the nasopharynx.

LESLIE, Evanston, Ill.

AN ENCEPHALTITIC SYNDROME WITH TRANSITORY BLINDNESS BUT WITHOUT OPHTHALMOLOGIC SIGNS IN TWIN GIRLS. A. GENTILI, Lattante **8**:286 (May) 1937.

These twins were identical. One, seen at the age of 16 months, had convulsions for a week. She became blind, although ophthalmologic examination revealed no abnormalities in the fundi. Four months later, she began to show signs of returning vision and in twenty days could see normally. She has continued to develop normally both intellectually and physically.

The second twin at the age of 2 months was taken sick with whooping cough. Convulsions followed, lasting about a week. She also lost the ability to see, although on ophthalmologic examination the fundi appeared normal. About two and one-half months later vision began to return and gradually became normal.

It is interesting that twins with encephalitis from two different causes should both show transitory blindness without ophthalmologic signs. It appears that these identical twins had a morbid predisposition toward involvement of the visual area of the brain and therefore had similar histories of blindness.

HIGGINS, Boston.

ENCEPHALOGRAMS IN PEDIATRICS. A. M. ABRIL and H. F. DE CASTRO, Arch. de med. inf. **6**:159 (June) 1937.

The subject is thoroughly reviewed, and forty-eight illustrative encephalograms are shown. They are important in establishing diagnosis, prognosis and occasionally therapeusis. Encephalography is harmless if the technic is correct. It should be preceded by a thorough neurologic examination, as intracranial hypertension is a strict contraindication. No conclusions can be drawn from a single encephalogram. Different positions must be checked.

SANFORD, Chicago.

THE DIAGNOSIS OF CEREBRAL TUMORS IN INFANTS. A. M. ABRIL, Arch. de med. inf. **6**:201 (June) 1937.

The syndrome of intracranial hypertension is headache, papilledema and vomiting. It should always be considered as having origin in a tumor unless there is proof to the contrary. The only other common causes of this syndrome are abscess of the brain and serous meningitis.

SANFORD, Chicago.

CEPHALOCELE ORBITAE ANTERIOR. A. MIKLÓS, Arch. f. Ophth. **137**:222 (June) 1937.

Miklós reports two cases of anterior cephalocele of the orbit (one case is that of a patient operated on by Kreiker and reported by him in 1922). Exploratory puncture is recommended to establish the diagnosis. Early operation is indicated unless the cephalocele is accompanied by more serious developmental defects or by hydrocephalus.

KRONFELD, Peiping, China. [ARCH. OPHTH.]

Diseases of the Genito-Urinary Tract

RENAL RICKETS. S. GOLDBERG and J. L. CANDIDO, Arch. Pediat. **54**:291 (May) 1937.

An Italian boy of 6 years who weighed 30 pounds (13.6 Kg.) and was 36 inches (91.5 cm.) in height is reported as presenting renal rickets. Besides the retardation in growth and emaciation, there was marked genu valgum. There were albuminuria and pyuria. Cystoscopy, ureteral catheterization and pyelography showed bilateral pyohydronephrosis and hydro-ureters. Roentgenographic examinations of long bones showed osteoporosis and rickets. Chemical studies of the blood revealed increased concentration of nitrogen. The blood calcium and phosphorus levels were normal. The child succumbed to diphtheria, and the observations at autopsy are submitted.

ORR, Buffalo.

THE ADDIS COUNT IN CHILDREN. H. H. BOYLE, C. A. ALDRICH, A. FRANK and S. BORORISKY, J. A. M. A. **108**:1496 (May 1) 1937.

Quantitative determinations of urinary sediment obtained by the Addis method were made in the cases of twenty-five children who had been clinically recovered from acute postinfectious hemorrhagic nephritis for periods of one-half to eight years. With the exception of one girl who was found to have hydronephrosis, the figures obtained corresponded with those obtained for normal children. In all other cases pathologic sediments were absent when ordinary clinical and laboratory methods gave normal reactions. This evidence points to earlier conclusions that children who clinically have recovered from this disease do not have latent or subacute nephritis.

BONAR, Salt Lake City.

UROLOGIC CONDITIONS IN CHILDREN. R. L. ANDERSON and J. J. LEE, Pennsylvania M. J. **40**:623 (May) 1937.

Until comparatively recent years it was not generally recognized that children were subject to urologic ailments similar to those of adults. Even today, in spite of modern methods of urologic diagnosis and treatment, such as cystoscopy, ureteral catheterization, pyelography and renal function tests, most general practitioners and many pediatricians and urologists fail to give proper attention to this phase of urologic practice. Close cooperation of the general practitioner, the pediatrician and the urologist in the investigation and treatment of pathologic conditions of the urinary tract occurring during infancy and childhood is desirable. The difficulty lies in convincing the attending physician, not the parents, that a

urologic examination is advisable. Some general practitioners still consider cystoscopy in a child a dangerous procedure and hesitate to have it done.

At the present time, with instruments made especially for children, it is possible to catheterize both ureters at the same sitting and to make a complete study under a single anesthesia. It is usually necessary to administer a general anesthetic to very young children, but girls as young as 4 and boys as young as 8 can be submitted to this examination with only local anesthesia. Cystoscopy and pyelography have the same importance in the study of urologic conditions in children as in adults, and the procedures are identical.

The authors review the treatment of anomalies, pyelitis, calculi, tumors and renal tuberculosis. In pyuria not rapidly responding to medical treatment the need for a urologic investigation is stressed.

LOGUE, Williamsport, Pa.

CONGENITAL POLYCYSTIC DISEASE OF THE KIDNEYS. H. R. SPENCER, South. M. J. **30**:524 (May) 1937.

A review of the history of this disease indicates that it is hereditary and results from embryologic maldevelopment. It occurs as often in one sex as in the other and in newly born infants or in adults in or past the third decade.

The symptoms are the result of progressive pressure atrophy of the renal parenchyma or of infection, and the diagnosis can be confirmed by the characteristic pyelogram.

The clinical findings are: a mass, urinary changes characteristic of renal failure, decreased excretion of phenolsulfonphthalein, a well tolerated retention of nonprotein nitrogen, intermittent hematuria and hypertension.

SCHLUTZ, Chicago.

ENURESIS IN CHILDREN: A REPORT OF SEVENTY CASES. H. C. MCGREGOR, Brit. M. J. **1**:1061 (May 22) 1937.

In this series of cases enuresis had been present since birth. Cases of enuresis in mentally deficient children were not included. In each instance examination failed to disclose any physical abnormality or any organic disease. The patient was presented with a small calendar to be kept by the bedside, on which the date of each dry night was to be recorded by him. A reward for success was offered in the earlier stages of the experiment, but it was found later that praise and encouragement were sufficient. If a child was unable to read figures, the parents had to record the results. No other treatment was used. Of course, when organic disease was present, that was corrected, and the aforementioned measures were adopted later. Cases are cited as examples and the status of the family is outlined, including social and economic factors.

The author feels very positively about the success of this very simple procedure.

ROYSTER, University, Va.

TREATMENT OF URINARY INFECTIONS WITH CALCIUM MANDELATE. E. SCHNOHR, Lancet **1**:1104 (May 8) 1937.

Treatment of eight patients with calcium mandelate gave the same good results as treatment with other preparations of mandelic acid. It has the great advantage of being tasteless and seldom causes dyspeptic symptoms.

LANGMANN, New York.

SPECIFIC SERUM IN THE TREATMENT OF COLON BACILLUS INFECTIONS OF THE URINARY TRACT. M. DE BIEHLER, Arch. de méd. d. enf. **40**:215 (April) 1937.

Infections traced to colon bacilli have been classified as endogenous and exogenous; an example of the former type may be seen when, through lowered immunity or through lesions of the mucosa induced by other diseases, these bacteria

are conveyed to adjacent or even remote organs; an exogenous infection may come from outside the body in contaminated food.

Frank septicemia, or the so-called colibacteremia of Michalowicz, may be provoked by direct passage of colon bacilli into the blood stream and may produce symptoms common to other septicemias. In infants, these invasions may resemble dysentery or enteritis; they may later extend to the liver, the pleura, the peritoneum or the urinary tract.

Kroguis was the first to recognize the possibility of renal infections with colon bacilli and Escherich pointed out ports of entry in the urinary system; in the female, entrance is found through the ureter and the genital organs; in the male, the bacilli pass from the intestine by way of the lymphatics; in both instances their invasion terminates in the bladder.

The question of ascending or descending infections is debatable, but in any case, according to Escherich, retention, weakness of the walls of the bladder and especially the action of toxins on the mucosa of the urinary tract are indispensable to the production of an infection with Bacillus coli in this area. Coincident infection with streptococci or the staphylococci is frequently found.

Serotherapy for colon bacillus infections was first used by Adam, Scheer and Lange; cultures from the intestinal tracts of infants in good health as well as from those of infants suffering from various diseases were employed. The serum was offered (1) in dyspepsia of nurslings, (2) after operative procedures, such as appendectomy, and (3) in acute and chronic disturbances of the urinary tract. Results have been satisfactory, the temperature often falling brusquely and the general discomfort being promptly ameliorated. Where the serum was not efficacious, careful search often revealed congenital malformations, lithiasis or hydronephrosis. De Bichler reports four cases in which treatment by anti-colon bacillus serum was successful.

AMESSE, Denver.

LIPOID NEPHROSES IN CHILDREN. P. NOBÉCOURT, Lattante **8**:243 (May) 1937.

Nobécourt summarizes present knowledge of lipoid nephrosis in children. As for prognosis, he concludes that one half of the patients die more or less rapidly, one quarter get well, and one quarter are lost from sight without the result being known.

HIGGINS, Boston.

DIFFERENTIAL DIAGNOSIS OF PROTRACTED PYELOCYSTITIS IN INFANTS AND CHILDREN. G. DUZÀR, Lattante **8**:255 (May) 1937.

The diagnostic and therapeutic procedures used in the hospital at Pécs in cases of persistent pyuria are outlined.

HIGGINS, Boston.

RENAL RICKETS WITH NEPHROSIS AND GLYCOSURIA BUT NORMAL BLOOD SUGAR. P. FORNARA, Lattante **8**:357 (May) 1937.

Fornara reports the case of a boy of 8 years with renal rickets and renal diabetes. At the age of 3 he had shown albumin in the urine and 2 per cent sugar; also white cells and granular casts; the blood sugar averaged about 0.09 per cent. As the child grew older, the albumin, white cells and casts persisted, but the glycosuria gradually disappeared. Photographs of the child reveal marked rachitic deformities.

HIGGINS, Boston.

HEMATURIA IN CASES OF HYDRONEPHROSIS. A. LOESCHKE, Kinderärztl. Praxis **8**:145 (April) 1937.

Seven cases of hydronephrosis are described in which mild, moderate or even severe hematuria was observed. Abdominal pains often accompanied bleeding but not necessarily. Infection of hydronephrotic kidneys predisposes to severe hemorrhage.

HEYMANN, Cleveland.

TREATMENT OF INFECTIONS OF THE URINARY TRACT WITH DERIVATIVES OF SULFANILAMIDE. A. WEISER, Med. Klin. **33**:674 (May 14) 1937.

Treatment of a large series of patients who had failed to respond to other therapy with derivatives of sulfanilamide (para-aminobenzene sulfanamide base) yielded almost universally good results, usually within forty-eight hours, regardless of the causative organism (except Bacterium tuberculosis and the gonococcus). The drug (in much greater concentration than that in which it is effective in vivo) is ineffective in inhibiting growth of the colon bacillus and the staphylococcus in vitro. Whether it has a direct or indirect effect on organisms in vivo has not yet been determined.

SIEMSEN, Chicago.

DIFFICULTIES IN ESTABLISHING THE SEX OF CHILDREN. R. J. HARRENSTEIN, Maandschr. v. kindergeneesk. **6**:299 (May) 1937.

This is an extensive discussion of difficulties in establishing sex, with some examples out of the author's practice. Exact examination of the patient should establish the sex, even if a laparotomy should be necessary. The author further mentions the measures to be taken in order to correct a wrong notice to the registrar.

VAN CREVELD, Amsterdam, Netherlands.

NEPHROSIS OR NEPHRITIS. L. MEYLER, Nederl. tijdschr. v. geneesk. **81**:2212 (May 15) 1937.

The histologic changes in lipoid nephrosis are mainly seen in the renal tubuli. The clinical picture, however, gives little evidence of disease of the tubuli and rather suggests an explanation by increased permeability of the glomeruli. It is questionable whether the turbid swelling and granular degeneration of the tubuli prove that the renal cells are diseased. By the investigations of Govaerts it has been made more probable that the tubular cells are not diseased but have merely absorbed protein and lipoid granules. There is increasing evidence in the literature that lipoid nephrosis in the course of years changes its picture to one typical of secondary nephrosclerosis. Four cases are described: In one patient the issue could be followed up regularly; uremia developed, and the patient died. The three remaining patients with lipoid nephrosis appeared to have acquired marked symptoms of chronic nephritis after fifteen, nine and six years, respectively. The author concludes that lipoid nephrosis is merely a special form of glomerular nephritis.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Ductless Glands; Endocrinology

OBSERVATIONS ON PROTAMINE ZINC INSULIN. R. RICHARDSON, Am. J. M. Sc. **193**:606 (May) 1937.

Diet.—Dietary care is fully as necessary with protamine zinc insulin as with insulin. A diet composed of 1 Gm. of protein per kilogram of body weight, an amount of fat equal to or slightly less than that found in the diet of the nondiabetic person (from 80 to 100 Gm. daily) and an amount of carbohydrate sufficient to provide the requisite number of calories daily will be found very satisfactory.

Examinations of Urine.—In order to check the balance between the protamine zinc insulin and the food, four specimens of urine may be collected, namely, one at 7 to 11 a. m., a second at 11 a. m. to 4 p. m., a third at 4 to 9 p. m. and a fourth at 9 p. m. to 7 a. m. Alteration of the amount of the protamine zinc insulin or of the amount or distribution of the food will bring about a satisfactory adjustment; such alteration must, of course, be based on the results obtained in the individual case.

Blood Sugar Determinations.—Blood sugar determinations need not be made until the urine contains no sugar, when a specimen of blood should be taken to determine, if possible, whether there is present a renal threshold above 180 mg.

If a renal threshold higher than this is found, examinations of urine cannot be depended on to maintain a satisfactory adjustment. When all specimens of urine are sugar free, further blood sugar determinations should be made from time to time.

Hypoglycemic Reactions.—A hypoglycemic reaction may occur following the use of protamine zinc insulin but less frequently and usually with less severity than after the use of insulin. It may appear at any time during the day or night, though it occurs most frequently at from twelve to twenty-four hours after the injection. The onset is slow and insidious as compared with that following insulin. This delay in development, however, affords sufficient opportunity to initiate treatment if the patient will but observe the approach of the reaction. It has been reported that reactions following the use of protamine zinc insulin have responded less readily to treatment than reactions caused by insulin.

Symptoms of hypoglycemic reaction sometimes do not occur even when the blood sugar is very low, but the patient should be warned by nervousness, weakness, sweating, drowsiness, headache, nausea, slight mental disturbances, tingling of the extremities, visual disturbances or any other unusual sensation.

Treatment of a reaction following injection of protamine zinc insulin consists in taking from 5 to 10 Gm. of dextrose or other sugar, such as orange juice, honey or cane sugar, dissolved in water. This should be followed by 5 Gm. of slowly absorbing carbohydrate, such as 2 saltine crackers, a dose which should be repeated at intervals of an hour until the succeeding regular meal. If the reaction is severe, from 10 to 20 Gm. of dextrose should be given intravenously. When in doubt about the approach of a reaction the patient had better take 5 Gm. of sugar and note the effect rather than allow the condition to proceed unchecked.

Prevention of hypoglycemic reactions is possible by exercising care as to the amount of protamine zinc insulin given and as to the distribution of food. The patient should also be warned about omitting or reducing meals or taking excessive exercise without a small amount of carbohydrate having been taken beforehand.

Storage of Protamine Zinc Insulin.—Protamine zinc insulin keeps well if properly cared for. Unopened packages should be stored in a refrigerator. Vials in use need not be kept cold but should be protected from heat, extreme cold or strong light.

Restrictions on the Patient with Diabetes.—Richardson has found that patients respond well if it is explained to them that their condition entails only two definite restrictions on their daily lives: (1) strict adherence to the diet and (2) the taking of one dose of protamine zinc insulin daily.

HENSKE, Omaha.

STATISTICAL SURVEY OF ENDOCRINOPATHIES AMONG YOUNG DELINQUENTS. N. M. TAYLOR and R. L. SCHAEFER, Endocrinology **21**:189 (March) 1937.

Taylor and Schaefer offer statistical data on the presence of various types of glandular imbalance among delinquent children. A survey was made of 2,311 children who passed through a juvenile court. The following specific diagnoses were utilized:

Thyroidism: (*a*) colloid goiter; (*b*) hypothyroidism; (*c*) hyperthyroidism.

Pituitarism: (*a*) dwarfism; (*b*) gigantism; (*c*) adiposogenitalism; (*d*) neurohypophysial obesity; (*e*) Simmonds' disease.

Gonadism: (*a*) hypogonadism; (*b*) hypergenitalism.

The incidence of endocrinopathies was 17 per cent, which is a frequency of 7 per cent greater than that in Engelbach's estimation of the distribution of glandular dysbalance in the general population.

The greatest number of cases occurred in the group with pituitary disorders. Hypothyroidism accounted for the greatest number of cases of a single endocrinopathy and represented the highest percentage of cases of endocrinopathies in girls. The groups of children with pituitary dwarfism included the greatest number of boys. Children with gonadism comprised about 14 per cent of the total number with glandular disturbances and included almost three and one-half times as many boys as girls. If the group of cases of probable endocrinopathies is added to those

in which a positive diagnosis was made, the percentage is raised to 24, or an increase of 140 per cent over Engelbach's estimated number of cases of glandular dysbalance in the total population.

An analysis of the figures presented reveals graphically that behavioristic problems are much more prominent during the years of adolescence and that these problems are definitely increased if the adolescent child has an associated endocrine imbalance.

JACOBSEN, Buffalo.

PROTAMINE INSULINATE IN JUVENILE DIABETES. H. M. FEINBLATT, B. ALPERT and E. A. FERGUSON, M. Rec. **145**:366 (May 5) 1937.

Formulas are recommended for changing from standard insulin to protamine insulinate and for calculating the optimal dose of protamine insulinate. The unit value of this drug is 20 per cent greater than the unit value of standard insulin.

The adjustment to protamine insulinate was established at the end of the third day. The intercipient use of standard insulin conflicted with the efficiency of the new protamine insulinate and was found to be unnecessary. Patients showed a constant gain in weight and marked improvement in fat metabolism. Absence of ketonuria and infrequency of lipemia were the rule.

WILLIAMSON, New Orleans.

ADRENAL HEMORRHAGE IN CHILDREN. W. M. FIROR, South. M. J. **30**:306 (March) 1937.

The author reports a case of fatal adrenal hemorrhage in an infant 13 months old. The child presented considerable gastro-intestinal bleeding, which led to the assumption that there might be a lesion in the stomach or a diverticulum or polyp in the intestinal tract. None of these conditions was observed at operation; at autopsy, however, an infected cavity in the pancreas communicating with the pancreatic duct was found to be the source of the bleeding into the gastro-intestinal tract, and extensive hemorrhage destroying both adrenals explained death.

The author discusses the probable theories underlying the development of such a condition. There is, at present, no therapy for this rare and uniformly fatal condition.

SCHLUTZ, Chicago.

THE LAURENCE-MOON-BIEDL SYNDROME—RECORD OF A CASE. J. R. MUTCH, Brit. J. Ophth. **21**:225 (May) 1937.

The patient's mother, one of a family of twelve, is living and healthy; two males are affected with atrophy of the retina and optic nerve. The patient is the third of five children, four being males and one a female. There was no parental consanguinity. The remaining two brothers and the sister are alive and normal.

The patient is aged 35. His vision became dim at the age of 12 years but later improved, only to fail again at the age of 30. Night blindness is not present. Vision is 6/60 in each eye. The fields are contracted and show a defect in the left upper temporal area. There is an indefinite central scotoma for red and green. He is not color blind. Each optic disk is pale and has sharp edges. There are a slight mottling at both maculae and a gray spot near the left macula but no pigmentary changes at the periphery. The other symptoms are: moderate obesity, hypogenitalism and hypospadias, mental retardation, polydactyly and syndactyly. The article is illustrated.

ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

ENDOCRINES IN THEORY AND PRACTICE: THE PARATHYROID GLANDS. D. HUNTER, Brit. M. J. **1**:929 (May 1) 1937.

This is one of a series of articles on endocrinologic subjects and is lucid and stimulating to read. It does not lend itself to abstracting and must be read in its entirety.

ROYSTER, University, Va.

THE PROBLEM OF GOITER IN CHILDHOOD. E WIELAND, Arch. f. Kinderh. **105**:129, 1935.

Goiter represents an increase in the physiologic growth of the thyroid gland at the time of increased development of the body and during the crises of female sex life. This increased growth is endemic in certain regions where it may be conceived of as a work hypertrophy for the purpose of producing a quantitatively and qualitatively sufficient iodine-containing specific secretion. The variations in the morphologic and functional character of goiter in individual regions in which it is endemic lead to the assumption of exogenous causes in addition to endogenous causes and apparently partly hereditary factors. The character of the drinking water has been emphasized as an important factor by nearly all investigators, whether as a cause of chronic intestinal infection or because of its content of radioactive substances or its lack of iodine. The general use of iodine salt in regions in which goiter is endemic is strongly recommended.

CRANE, Chicago.

GOITER IN NEW-BORN INFANTS AND IN CHILDREN. LUDWIG ASCHOFF, Arch. f. Kinderh. **105**:159, 1935.

The average weight of the thyroid gland of new-born infants in the German goiter regions is almost double that for new-born infants in goiter-free regions of Germany. Both goitrous and normal thyroid glands are larger at birth than they are six months later. The larger thyroid gland of the new-born in goiter regions consists histologically of an increase in parenchyma and is probably due to the same exogenous factor — lack of iodine — which causes other goiter in these districts. Calculations from the author's own material (Baden) indicate that in 10 per cent of infants dying at birth or shortly after death was due to pressure from an enlarged thyroid gland. In later childhood and in the period preceding puberty enlargement of the thyroid gland in the form of diffuse colloid struma is common in the goiter regions; nodular goiter is less common but is also observed in children from 10 to 12 years or older.

CRANE, Chicago.

OBSERVATIONS ON THE ADRENALIN NEED IN MAN AND THE EFFECT OF ADRENALIN ON THE BLOOD PRESSURE AT DIFFERENT BLOOD-PRESSURE HEIGHTS. C. GRILL, Acta med. Scandinav. **91**:628, 1937.

In a case of Addison's disease a therapeutic experiment was performed with epinephrine in intravenous infusion. By this method the blood pressure could be raised from 75 systolic and 50 diastolic to 120 systolic and 80 diastolic, as measured in millimeters of mercury, and kept there for about forty hours. No perceptible improvement was observed in the general condition. When the supply of epinephrine was stopped, the blood pressure fell again, the general condition declined and the patient died in twenty-four hours.

Autopsy revealed that both adrenal glands were completely destroyed by a caseous tuberculous process.

The amount of epinephrine required to maintain normal blood pressure in the patient agreed well with the amount of normal secretion established in animals.

Before the experiment injection of 0.5 mg. of epinephrine intramuscularly failed to raise the blood pressure, but during the experiment the same dose produced a rise of 30 mm. of mercury. The reduced sensitivity to epinephrine in Addison's disease is therefore only apparent.

After injection of epinephrine, the most marked rise in blood pressure was noted when the initial blood pressure was 115 mm. of mercury. The more the blood pressure varies above or below 115 mm., the less will be the effect of epinephrine.

KAJDI, Baltimore.

Treatment of Diabetes with Insulin and Epinephrine. V. Clausen and M. C. Lottrup, Ugesk. f. læger **97**:747 (July 18) 1935.

The addition of small quantities of epinephrine to insulin retards its resorption. Such a combination (0.02 to 0.04 mg. of epinephrine-hydrochloride per cubic centimeter of insulin) has a more even and lasting effect on the glycemia in diabetic patients than has ordinary insulin. It is easier to avoid great fluctuations of the blood sugar content and sometimes only one injection is needed instead of two.

Wallgreen, Göteborg, Sweden.

Adrenal Apoplexy. S. van Creveld, Maandschr. v. kindergeneesk. **5**:102 (Dec.) 1935.

A case is reported of the Waterhouse-Friderichsen syndrome observed in a boy of 7 months. A description is given of the symptoms and pathologic picture and a disucssion of the results of chemical and morphologic examination of the blood in analogous cases. As regards therapy for the syndrome, with its rapid course, both extract of the adrenal cortex and epinephrine are advised. Next to these, injections of dextrose and sodium chloride and eventually blood transfusions are recommended, and according to the present conception of the etiology, the (intravenous) injection of anti-meningococcus serum must also be seriously considered.

van Creveld, Amsterdam, Netherlands.

Influence of Zinc on the Activity of Insulin. L. A. Hulst and E. H. Vogelenzang, Nederl. tijdschr. v. geneesk. **81**:1916 (May 1) 1937.

The work of Scott and others in experiments on animals and especially that of Rabinowitch on human subjects in relation to the action of zinc insulin and of protamine zinc insulin raised the problem of the nature of the action of zinc apart from that of insulin. In the fasting diabetic subject zinc was shown to raise the blood sugar level. If zinc and insulin are injected separately at the same time the deepest point of the sugar curve is delayed and maintained for a longer time; if zinc and insulin are mixed before injection the beginning of the effect is moreover delayed.

van Creveld, Amsterdam, Netherlands.

Diseases of the Muscles, Bones, Joints and Lymph Glands

Fragilitas Ossium with Otosclerosis and Blue Scleras: Report of a Case. A. A. Cinelli, Arch. Otolaryng. **25**:309 (March) 1937.

Cinelli reports the case of a 34 year old man, concluding that disturbances of the mesenchyme from which the fibrous and osseous tissue developed are responsible for the pathologic condition. The 2-A audiometer showed 42 per cent loss of hearing on the left side and 50 per cent loss on the right side.

Greenwood, Chicago.

Use of Homologous Bone Grafts in Cases of Osteogenesis Imperfecta. A. De Forest Smith, Arch. Surg. **34**:687 (April) 1937.

In view of the fact that not in all cases of osteogenesis imperfecta does the lesion heal without difficulty, attempts were made to correct the deformities by using homologous bone grafts from the tibias of donors. The author cites his experience with four patients with ununited fractures and severe deformities of the bones of the lower extremities which completely prevented walking. These were all treated with onlay bone grafts from the tibias of donors. The operations were successful in correcting the deformities, and hypertrophy of the bones enabled the patients to walk. It is believed that a homologous bone graft can be used to advantage in such cases.

Kaiser, Rochester, N. Y.

ROENTGEN RAYS IN THE TREATMENT OF ACUTE CERVICAL ADENITIS. S. HURWITZ and S. N. ZUKERMAN, J. Pediat. **10**:772 (June) 1937.

Sixty-two infants and children suffering from acute cervical adenitis were treated with roentgen rays. Twenty-one of these patients were hospitalized, and forty-one were treated in the outpatient clinic. The dosage used on the patients in the hospital was from 10 to 20 per cent of the skin erythema dose, repeated every three to five days. Treatment was begun from two to twenty-eight days after the onset, the average time being eight and three-tenths days. The number of treatments ranged from one to five. Resolution occurred in seventeen (80.9 per cent) of the roentgen-treated patients as opposed to ten (58.8 per cent) in a controlled group. Suppuration resulted in three (14.3 per cent) of the roentgen-treated patients, while seven (41.2 per cent) of the controlled group showed abscess formation. Among the children treated in the outpatient clinic, on whom a dose of from 70 to 200 roentgens was used, from one to three treatments, at intervals of from two to seven days, were found sufficient to bring about resolution in thirty-five (85.4 per cent). Suppuration occurred in six patients (14.6 per cent). The striking features of this method of treatment were rapid subjective improvement and accelerated termination. Radiation was most beneficial in the early stages of inflammation, absorption being the usual final result. In cases in which suppuration had already occurred, radiation hastened necrosis and early centralization of infection, thus minimizing surgical intervention and enhancing the cosmetic effect.

RAUH, Cincinnati.

ACUTE HEMATOGENOUS OSTEOMYELITIS WITH ADJACENT JOINT INFECTION. R. C. ROBERTSON, South. M. J. **30**:503 (May) 1937.

Robertson discusses eighty cases of acute suppurative hematogenous infectious osteomyelitis, in twenty of which adjacent suppurative arthritis was present on first examination. Aspiration of the involved joint is of great value in early diagnosis. Involvement of the adjacent joint aids decompression of an infected bone; hence early incision drainage of the joint is the preferred treatment both for the joint complication and the underlying bone lesion. When drainage is obtained in an early stage, the prognosis for preservation of joint function is good.

SCHLUTZ, Chicago.

POSTURAL DEFORMITIES OF THE ANTEROPOSTERIOR CURVES OF THE SPINE. P. WILES, Lancet **1**:911 (April 17) 1937.

The conclusions which Wiles draws from his study are (1) that the regulation of posture is a function of the central nervous system, which determines the length at which the muscles are habitually held, the strength of the muscles being of less importance, and (2) that the pelvic inclination is regulated by the muscles surrounding the hip joint and not by the trunk muscles.

A new instrument is described for measuring the pelvic inclination.

The importance of rapid growth, undernutrition and psychologic factors in the etiology of postural deformities is emphasized. Final correction of a deformity is brought about by establishing new postural reflexes. This is never done by movement but only by the absence of movement. Exercises are designed to keep the parts of the body concerned, still.

LANGMANN, New York.

A CONTRIBUTION TO THE PATHOLOGY OF THE RHEUMATOID TYPE OF ARTHRITIS AND OF RHEUMATIC FEVER. A. G. T. FISHER, Lancet **1**:1162 (May 15) 1937.

This study is based on examinations of synovial tissues removed at operations and of pathologic changes in the articular cartilage and bone seen in the later stages of the disease.

With Klinge the author maintains that the fibrinoid degeneration of the synovial membrane is an important feature of the rheumatoid type of arthritis of so-called

unknown etiology and that this form of degeneration is not, therefore, confined to acute rheumatism. In the latter condition it is seen not only in the synovial membrane but in the heart and in other regions affected by the disease.

The author's investigations showed that this form of degeneration was a characteristic feature of rheumatoid arthritis of unknown etiology except in the very early and in the more chronic stages. LANGMANN, New York.

THE B. I. P. P. METHOD OF TREATMENT OF ACUTE OSTEITIS. J. H. SAINT, Lancet **1**:1211 (May 22); 1263 (May 29) 1937.

Saint applies the term "osteitis" to inflammation of any or all of the constituent parts of a bone. The disease begins as a small delimited focus of infection in the cancellous tissue of the metaphysis. This focus can be completely removed, and its removal constitutes the rational treatment.

Stress is laid on the necessity for early diagnosis. The triad of continuous pyrexia, intense pain of sudden onset over the metaphysis of a long bone, and exquisite tenderness on palpation of the same region, associated with polymorphonuclear leukocytosis, are the clinical features that appear early and establish the diagnosis.

Numerous claims are listed for the treatment of acute osteitis with bismuth-iodoform-paraffin paste, among which are the low mortality rate, the simple technic, the painlessness of the dressings and the infrequent need of redressings.

LANGMANN, New York.

CONGENITAL DISLOCATION OF THE PATELLA POSTERIORLY. J. L. MENCIERE, Rev. d'orthop. **24**:239 (May-June) 1937.

A boy of 12 years was admitted to the hospital for operation. The left leg showed a rotation of the tibia and fibula on the femur of about 90 degrees. The patella was displaced laterally so that it lay almost in line with the posterior line of the femur. The boy could walk with the aid of canes. The condition had been present from birth. In all cases of congenital dislocation of the patella there is some accompanying rotation of the lower part of the leg, but the 90 degrees observed in this case is extreme.

Correction was performed in two stages. In the first, the patella was replaced in proper position and held there by the technic of Mouchet. At a later date the rotation of the tibia and fibula was corrected by an osteotomy through the line of attachment of the tubercle in the tibia and slightly lower in the fibula. Excellent results were obtained.

At the present time the patella remains in place, and the axis of the leg is normal, the foot directed anteriorly. The genu valgum has almost disappeared, all motions of the knee have been maintained, and the boy is able to stand on his toes and walk without aid. RYAN, Vancouver, B. C.

LYMPHOBLASTIC SARCOMA OF THE MESENTERIC GLANDS IN A BOY OF TWENTY-TWO MONTHS. E. ZECCA, Lattante **8**:309 (May) 1937.

Zecca presents a fatal case, together with the observations at autopsy, of lymphosarcoma involving the mesenteric glands in a child of 22 months. The outstanding finding was marked distention of the abdomen with ascites. The ascitic fluid was opalescent and contained emulsified fat. HIGGINS, Boston.

CONGENITAL RELAXATION OF THE DIAPHRAGM. G. COSACK and J. WIENBECK, Monatschr. f. Kinderh. **70**:161 (May) 1937.

This is a report with x-ray pictures and observations at autopsy on a condition which the writers call congenital relaxation of the diaphragm. The symptoms and findings are identical with those of diaphragmatic hernia. The differential diagnosis

is important because the hernia may be influenced by operation. The x-ray picture is of great assistance in showing the perfectly symmetrical outline of the congenital relaxation.

Various theories as to the morphogenesis are discussed.

GERSTLEY, Chicago.

FENESTRAE PARIETALES SYMMETRICAE. R. VOIGT, Monatschr. f. Kinderh. **70**:224 (May) 1937.

A case is reported and roentgenograms are reproduced of a child in a family with cranial defects. Voigt attempts to show that these defects are hereditary and may be related to cerebral dysplasia. He suspects that they may also be classified as types of spina bifida.

GERSTLEY, Chicago.

Skin Diseases; Allergy

SHOES: A SOURCE OF REINFECTION IN RINGWORM OF THE FEET. R. C. JAMIESON and A. MCCREA, Arch. Dermat. & Syph. **35**:203 (Feb.) 1937.

Cultures of insoles of the shoes of patients with ringworm of the feet were taken, and 30 per cent gave positive results for pathogenic organisms. Of fifty-two cases tested, pathogenic organisms or organisms suspected of being pathogenic were recovered in thirty-five cases. Even with this high percentage of positive results the authors feel that it is the persistence of the organisms in the tissues of the feet that leads to reinfection. Some dermatologists feel that this is rather too conservative a statement. The authors conclude the article with the following: "It appears that shoes are not a probable source of infection or reinfection but should be definitely considered as a potential source of infection especially if worn by non-infected persons."

DULIN, Iowa City.

INFLUENCE OF AVITAMINOSIS A ON EXPERIMENTALLY PRODUCED CUTANEOUS INFECTIONS IN RATS. T. H. STERNBERG and D. M. PILLSBURY, Arch. Dermat. & Syph. **35**:247 (Feb.) 1937.

In experiments conducted by the authors, albino rats with vitamin A deficiency showed no less resistance to skin infections than normal controls. Both streptococci and staphylococci were used and attempts made to produce infections by intradermal injection and contamination of scarified skin with pure cultures. Though some of the rats were dying of vitamin A deficiency (loss of weight and xerophthalmia), they showed rapidly healing infections at the sites of inoculation.

DULIN, Iowa City.

ERUPTION RESEMBLING LICHEN SCROFULOSORUM COINCIDENT WITH NONTUBERCULOUS PULMONARY DISEASE. E. T. BERNSTEIN, Arch. Dermat. & Syph. **35**:255 (Feb.) 1937.

Bernstein reports the case of a boy of 9½ years with lichen spinulosus in which the eruption resembled that of lichen scrofulosorum. It occurred with pulmonary disease, which added to the suspicion of lichen scrofulosorum. However, tuberculin tests were always negative, and on reviewing the history it was found that the pulmonary disease followed tonsillectomy; it was felt that this was a typical case of postoperative pulmonary abscess. Histologic studies at various stages of the eruption led to the final diagnosis of lichen spinulosus.

DULIN, Iowa City.

Eczema in Infants and Children. H. Goodman and M. Burr, Arch. Pediat. **54**:153 (March) 1937.

Goodman and Burr submit diets low in sugar as a means of preventing eczema.

Orr, Buffalo.

Congenital Ectodermal Defect. A. Capper and N. M. Bekir, Arch. Pediat. **54**:160 (March) 1937.

Two cases of congenital ectodermal defect are reported. In one case the condition existed in a mulatto girl 6 years old. She belonged in the anhidrotic group, as she never perspired and was subject to attacks of hyperpyrexia. She had no real hair, sparse eyebrows and eyelashes and brittle nails. Practically complete anodontia existed. The right lateral lower incisor was the only tooth present. Roentgen examination on two occasions failed to reveal any unerupted teeth. Careful inquiry into the patient's genealogy revealed no evidence of hereditary transmission.

The second case is that of a white boy 7 years old who belonged in the hidrotic group. The finger-nails and toe-nails covered only the proximal half of the nail bed. All his teeth were present. He had eyelashes and eyebrows. The hair on his scalp was sparse.

A genealogical chart shows the occurrence of this ectodermal anomaly in four generations. From this chart Capper and Bekir make the interesting observation that the defect can be transmitted by both males and females and can affect both sexes, though the incidence is greater among females.

Orr, Buffalo.

The Skin Reaction of Infants and Children to Soaps. L. Goldman, J. A. M. A. **108**:1317 (April 17) 1937.

A study was made of the cutaneous reactions of 127 children, 82 of whom were new-born, to seven common toilet soaps. Patch tests and swabbings with soap solutions were used. No changes were observed grossly after the latter. Newborn infants reacted much less frequently to the patch test than older infants and children. There was little difference in the reactions of the various soaps save one containing cresol.

Bonar, Salt Lake City.

Immunologic Relationship Between Grass Pollen and Seed. L. Farmer, J. Allergy **8**:338 (May) 1937.

As a result of experiments conducted on twelve patients known to be sensitive to the pollen of timothy Farmer concludes: "Although a close immunologic relationship between the pollens of different grasses may be assumed, it has been shown in the foregoing and in earlier experiments that there is no immunologic relationship between the pollens and seeds of the same plant, in spite of their close biological relationship."

Hoyer, Cincinnati.

Interruption of the Asthmatic Crisis by Tribromethanol (Avertin). A. M. Fuchs, J. Allergy **8**:340 (May) 1937.

Gratifying results were obtained in twenty-five adult patients following the use of tribromethanol in doses of from 50 to 70 mg. per kilogram per rectum. The patients were in a state of asthma and had not responded to the usual medication of ephedrine, epinephrine, dextrose, sodium iodide, etc. Under treatment with the anesthetic they would sleep from one to six hours and be free from asthma for days and even weeks. When it occurred subsequently, they would respond to the usual medication. The refractoriness to epinephrine was lost.

Hoyer, Cincinnati.

ALLERGY IN DERMATOLOGY: A CRITICAL REVIEW OF SOME RECENT CONTRIBUTIONS. M. B. SULZBERGER and J. GOODMAN, J. Allergy **8**:385 (May) 1937.

While the review may be intended primarily for the allergist, it contains much of value for the pediatrician interested in allergy. It is unbiased and contains an extensive bibliography.

The reviewer calls attention to Rackemann's admonition to all interested in allergy that an accurate complete history is of great importance and is essential for practical success.

HOYER, Cincinnati.

THE THRESHOLD OF TOLERANCE IN CUTANEOUS ECZEMA. E. LORTAT-JACOB, Paris méd. **1**:477 (May 29) 1937.

The author feels from his experience that eczema is due to a disturbance of the equilibrium of the vagosympathetic system which lowers the threshold of cutaneous sensitivity. The equilibrium may be upset by endocrine dysfunction or by a direct attack on the vagosympathetic system by an infecting organism.

LESLIE, Evanston, Ill.

ALLERGIC DIATHESIS. V. BAPTISTA, J. de pediat., Rio de Janeiro **4**:102 (March) 1937.

Baptista considers that there are three manifestations of the allergic diathesis: the cutaneous, as typified by eczema, neurodermatitis and urticaria; the mucosal, as typified by asthma, spastic colitis, rhinopharyngitis and the exudative diathesis, and finally, the internal manifestations, which are eosinophilia, spasm and vagotonia.

SANFORD, Chicago.

THREE CASES OF ERYTHRODERMIA EXFOLIATIVA. K. YAJIMA, J. Orient. Med. **26**:441 (March) 1937.

Diagnosis of so-called erythrodermia exfoliativa universalis is generally difficult, since this condition lacks uniformity in etiology and symptomatology. Yajima reports one case of dermatitis exfoliativa subacuta (Brocq) in a 26 year old woman and two cases of dermatitis exfoliativa secundaria subacuta, in a 31 year old woman and a 33 year old man, respectively. The entire bodies of these three patients were covered with scarlatinal, lamellar eruptions, with evidence of atrophy of the skin. In one case the scalp hair, nails and teeth had fallen out, and all three patients had a recurrence of symptoms each year. Histologically the lesions showed acanthosis, hyperkeratosis and irregularity of papillae, infiltration by round cells around hair follicles and widening of capillaries in the subpapillary layer; slight cellular infiltration in the neighborhood of sweat and sebaceous glands; increase in pigment in the basal layer and some atrophic appearance in all the layers. These changes simulated those seen in pityriasis rubra (Hebra). There were slight eosinophilia with leukocytosis but no lymphocytosis. The liver and pancreatic functions (as studied by the galactose tolerance test, Takata's serum reaction and Wohlgemuth's diastase test) were all normal.

KATO, Chicago.

CALCINOSIS UNIVERSALIS. J. J. C. P. A. ROOVERS, Nederl. tijdschr. v. geneesk. **81**:2346 (May 22) 1937.

A case is described, in a girl of 5 years, of generalized calcinosis in which recovery ensued after treatment with sodium citrate (3 Gm. a day) and calcium. No claim is made, however, from an etiologic standpoint.

VAN CREVELD, Amsterdam, Netherlands.

DERMATITIS BULLOSA CAUSED BY PETROLEUM. A. J. VAN KEKEM, Nederl. tijdschr. v. geneesk. **81**:2515 (May 29) 1937.

Kekem describes a girl of 8 years with dermatitis bullosa on the abdomen where the skin had been in close contact with petroleum.

VAN CREVELD, Amsterdam, Netherlands.

Surgery and Orthopedics

CARE OF THE SEVERELY BURNED. E. C. PODGETT, Arch. Surg. **35**:64 (July) 1937.

Podgett in a study of severely burned persons brings out the fact that for the first day or so the systemic changes assume a position of greater importance than the local injury. The systemic treatment should include administration of an adequate amount of morphine for the alleviation of pain and replacement of the lost plasma, which tends to accumulate in the tissues adjacent to the burned area. Hypotonic saline solution serves best for the purposes of dilution and replenishment of the fluids. To replenish the protein lost from the circulatory fluids autogenous blood is considered the solution nearest to that of the normal fluid. In the case of children with some evidence of acidosis, administration of a 5 per cent solution of dextrose is considered advisable. Transfusions of blood are given, the number according to the probable degree of the loss of plasma. When the oxygen-combining power of the blood is lowered, sodium bicarbonate is given in sufficient quantities to turn the urine alkaline. Usually after the first forty-eight hours, the systemic treatment consists in maintaining a relatively high intake and output of fluid. The article goes on with the local care of the burn and the various methods of skin grafting.

KAISER, Rochester, N. Y.

IMPORTANT OBSERVATIONS ON DEFORMITIES OF CHILDHOOD. H. KELLER, M. Rec. **145**:290 (April) 1937.

Keller emphasizes the following important points: 1. Since childhood is the period of rapid growth and of mental and physical development and since the necessary harmonious physicomental adjustment is greatly hampered by deformities in the child, it is one's duty to correct deformities as early as possible in the child's life.

2. Every deformity in a child needs careful study as to causative factors, and the problems entering into the corrective and therapeutic procedures differ greatly from those of adults.

3. Asymmetry of the lower limbs is found in the Near East, and though it is not as frequent in this country, yet it is found in a great number of children, and may be the causative factor in a good many deformities.

4. In many of these children with asymmetry of the lower limbs the upper limbs may also show inequality, and this probably indicates that one is dealing with congenital defects.

5. Mild infantile paralysis involving only the muscles of the back or the plantar region of the foot may often be overlooked. Lack of recognition and wrong treatment may be the cause of deforming contractures and complications which could easily have been prevented had proper measures been instituted at the beginning. If sudden flatfoot or mild scoliosis makes its appearance in childhood, a thorough examination should be made.

WILLIAMSON, New Orleans.

NATURE OF DIET IN ITS RELATIONSHIP TO CONTROL OF DENTAL CARIES. J. D. BOYD, C. L. DRAIN and G. STEARNS, Proc. Soc. Exper. Biol. & Med. **36**:645 (June) 1937.

Three children with dental caries and two control subjects without caries were studied in the metabolic ward under various dietary, vitamin D and vitamin A intakes over a period of seven months. Addition of vitamin D seemed to cause arrest of decay even though various control diets caused some decrease in the activity of the caries. In a subject who was being studied with regard to the influence of vitamin A on dark adaptation it took nine weeks for the administration of viosterol to cause complete arrest of activity in dental caries. It seems that a stage of near-arrest may be obtained with moderate control of the diet. The level of vitamin D seems to be the determining factor.

HANSEN, Minneapolis.

PLASMA PHOSPHATASE AND PHOSPHORUS DURING THE HEALING OF FRACTURES IN CHILDREN. O. D. PEDEM, Arch. Dis. Childhood **12**:87 (April) 1937.

The plasma phosphatase and the serum phosphorus and calcium were estimated at various intervals after a fracture injury in children. The plasma phosphatase appeared to increase within the first few days and thereafter to decrease. The serum phosphorus reached a maximum at the end of the first week. The serum calcium was not significantly altered. The change in plasma phosphatase was most marked in fracture of the femur.

KELLY, Milwaukee.

ANAESTHESIA FOR HARE-LIP AND CLEFT PALATE OPERATIONS ON BABIES. P. AYRE, Brit. J. Surg. **25**:131 (July) 1937.

Ayre found that nitrous oxide-oxygen anesthesia was not suitable for infants. In the first place, anoxemia was caused by nitrous oxide and, second, it was extremely difficult to adjust the amount of rebreathing to the small proportions suitable for a baby. He devised the following method:

Briefly, the apparatus consists of a T piece which is connected by a short piece of rubber tubing and a Magill angle piece to a wide bore Magill rubber catheter previously inserted into the trachea. Through one limb of the T piece oxygen and ether vapor is delivered from a Boyle or other continuous flow apparatus. The other limb remains open to the outside air; for convenience, a short piece of tubing may be attached and allowed to hang down beneath the operating towels. A strand of fine gauze fixed with adhesive strapping close to the open end of the latter tubing will wave to and fro with the patient's respirations, thus serving as a useful indicator to the anesthetist.

The advantages of this technic are: 1. The baby inhales fresh air and oxygen under as nearly normal physiologic conditions as possible, as the system is open to the outside air, without the intervention of anything, such as a rebreathing bag. 2. The "dead space" is reduced to negligible proportions, while the continuous flow of oxygen at the rate of from 1.5 to 3 liters a minute flushes out the lungs and effectually prevents undue accumulation of the products of respiration.

SUMMERFELDT, Toronto, Canada.

VOLVULUS OF THE WHOLE SMALL INTESTINE. STURROCK, Obst. Soc. Edinburgh, 1935, p. 62, in Edinburgh M. J. May 1935.

At 18 hours of age a boy became pale and cold and began to whimper. He would not nurse but took sweetened water. Only meconium passed, but in another eighteen hours there was bloody vomitus. At 40 hours of age the infant died. The entire small intestine was found to be purple and distended with blood; the peritoneal cavity likewise contained some bloody material. The small intestine was found to have rotated five times around the narrow pedicle formed by the base of the mesentery, which was only ½ inch (1.27 cm.) in length. Developmental rotation of the intestine had taken place, but the cecum was descended.

NEFF, Kansas City, Mo.

A CASE OF PHLEGMA ALBA DOLANS. M. GARCIA, Arch. de pediat., Rio de Janeiro **9**:341 (June) 1937.

This developed in the left arm of a 9 year old boy, following a minor infection of the skin. The treatment consisted in immobilization of the arm during a period of 40 days. Recovery occurred.

SANFORD, Chicago.

COMPLICATIONS DUE TO MECKEL'S DIVERTICULUM. E. NEUMANN, München. med. Wchnschr. **82**:655 (April 25) 1935.

Meckel's diverticulum may cause strangulation of the ileum or a hernia. At all operations for appendicitis in which the appendix is found to be normal the lower

end of the ileum should be examined for a possible diverticulum. The condition may occur at any age. The author's youngest patient was 5 years of age, and the oldest, 69 years.

BRAHDY, Mount Vernon, N. Y.

A CASE OF TORSION OF THE STOMACH. ÅKE RYDÉN, Hygiea **97**:257 (April 15) 1935.

A girl of 5 years, who had earlier been healthy, fell ill with abdominal pains and vomiting. There was no fever. Two days later a rounded orange-sized tumor was felt in the upper part of the abdomen, and the general condition was poor. A laparotomy was done. The tumor was found to be formed by the enormously distended stomach, which was torqued 360 degrees. The torsion had been brought about by relaxation of the diaphragm. The child left the hospital three weeks later in good health, with remaining relaxation of the diaphragm.

WALLGREN, Göteborg, Sweden.

PREVENTIVE THERAPY AND ORTHOPEDICS IN CHILDREN, WITH SPECIAL CONSIDERATION OF CONGENITAL MALFORMATIONS. R. J. HARRENSTEIN, Maandschr. v. kindergeneesk. **4**:403 (July) 1935.

In this article attention is drawn to the preventive measures which should be taken to prevent surgical and orthopedic operations on the child and to diminish as much as possible the risk of these operations. The period of life and the state of the disease which are most suitable for treatment are described. A systematic treatment of chronic illnesses, such as surgical tuberculosis, is advocated.

VAN CREVELD, Amsterdam, Netherlands.

A CASE OF CONGENITAL STRANGULATED DIAPHRAGMATIC HERNIA. P. M. E. P. NYST, Nederl. tijdschr. v. geneesk. **79**:3545 (July 20) 1935.

A case of this condition, so-called pleuroperitoneal hernia, in a boy of 1½ years old, is described. Abdominal operation was performed, with success.

VAN CREVELD, Amsterdam, Netherlands.

Teeth and Dentistry

USE OF ROENTGEN RAYS IN THE PRACTICE OF CHILDREN'S DENTISTRY. H. C. FIXOTT, J. Am. Dent. A. **24**:91 (Jan.) 1937.

Care of children's teeth and education of the children in the value of oral health and cleanliness and in methods of keeping the mouth and teeth clean are of primary importance for prevention throughout the whole field of dentistry.

The United States Public Health Service in Oregon found 91 per cent of elementary school children needing dental attention; 50 per cent showed malocclusion; 30 per cent of those reaching the age of from 12 to 14 years were recommended for orthodontic treatment.

Roentgen rays show from 25 to 40 per cent more caries in children's teeth than is noticed by visual and tactile examination alone. Intelligent diagnosis requires periodic roentgenographic examination.

"Some of the more common abnormalities of tooth development not discovered until too late without the use of roentgen rays are caries, congenital absence of teeth, the presence of supernumerary or impacted teeth, periapical infection, the presence of cysts and conditions involving the investing tissues of the teeth." Profile roentgenograms are also of frequent assistance and "should be used more often." Illustrations accompanying the article emphasize the importance of the use of roentgenograms in children's dentistry by showing the serious results of the lack of their use; an illustration is given for each of the abnormalities listed as not discernible without roentgenograms.

STEADMAN, Minneapolis [ANGLE ORTHODONTIST].

TREATMENT OF BURNS BY APPLICATION OF VITAMIN A. A. CHEVALLIER, F. CARCASSONNE and LUCCIONI, Progrès méd., Jan. 16, 1937, p. 89.

Extensive burns were treated by applications of vitamin A in cod liver oil. This was first applied following cleaning of the burn, with removal of the dead tissue, and was alternated with methylthionine chloride. The areas were exposed to the air, but no special mention is made of neighboring light bulbs.

The authors feel that this method of treatment produces more rapid cicatrization of the burn, with formation of more supple scar tissue than occurs with other methods. During the acute stage the general condition of the patient also seems improved under this treatment, and the fall in temperature is more rapid than is often seen.

LESLIE, Evanston, Ill.

SELF-CLEANSING OF THE MOUTH. J. BOL, Nederl. tijdschr. v. geneesk. **81**:2496 (May 29) 1937.

Examination of the saliva of fifty-three persons showed a constant rise of the alkali content after ingestion of an orange or a tart apple; the quantity of saliva was raised in three fourths of the cases. This is important for the self-cleansing of the mouth, a continuously increased amount of saliva with raised alkalinity providing a more efficient neutralization of the caries-producing acids. This is not the case with the large quantities of alkali applied in cleansing the mouth with tooth-paste, which impair the self-cleaning and damage the teeth and gums.

VAN CREVELD, Amsterdam, Netherlands.

Miscellaneous

OBSCURE FEVER IN EARLY LIFE. W. W. QUILLIAN, Arch. Pediat. **54**:304 (May) 1937.

Quillian reports a case.

ORR, Buffalo.

STUDIES ON ADAPTATION. H. SELYE, Endocrinology **21**:187 (March) 1937.

A reaction is described under the name "alarm reaction" which represents a nonspecific response of the organism to damage as such. Its main symptoms are: enlargement of the adrenals, involution of the lymphatic organs, degeneration and death of cells in various tissues, ulcer formation in the digestive tract and edema. These symptoms are the same whatever the specific nature of the damaging agent may be. Drugs, surgical injuries, spinal shock or excessive muscular exercise—all elicit the same reaction.

Experiments on rats show that if the organism is exposed daily to a stimulus causing an alarm reaction in the beginning, it will eventually become adapted to this stimulus. This adaptation, however, is lost after some time, apparently because the organism runs out of something needed for the fight against the damaging agent. At this time the animal dies in a condition of exhaustion, with symptoms similar to those seen in the acute stage of alarm. The whole reaction of adaptation consists, therefore, of three phases: the stage of alarm, the stage of resistance and the stage of exhaustion. Evidence is advanced which seems to support the hypothesis that the symptoms seen in the stage of alarm are due to the liberation of a histamine-like substance.

Selye remarks that it is difficult at first to understand why the organism should react to entirely different stimuli in an identical manner. The presence of a hypothetic substance having pharmacologic actions like those of histamine, although not necessarily chemically related to it, would explain the types of reaction seen here.

The effects of thyroidectomy and gonadectomy in modifying the response to damaging stimuli are discussed. The hypothesis is put forward that the factor necessary for adaptation, "the adaptation energy," is present in every person in a limited quantity only.

JACOBSEN, Buffalo.

A New Double Telescoping Cannula for Continuous Intravenous Therapy. S. Karelitz, J. Pediat. **10**:396 (March) 1937.

A double or telescoping cannula for continuous intravenous therapy is described and a drawing included. The cannula consists of an outer cannula, of 18 gage, and within it another cannula, of 21 gage—both made to fit the same adapter. The double cannula has great advantage over a single cannula. If a blood clot obstructs the flow of fluid, the inner cannula may be removed, cleansed and reinserted. The small gage of the inner cannula causes the pressure exerted by the column of fluid above it to become greater, thus lessening the danger of back flow of blood into the cannula and clot formation. The smaller cannula may be employed alone when a small vein is used. The rate of flow into the vein may be varied by the use of either an inner or an outer cannula; this is of special value in giving blood transfusions, for frequently if the flow of blood is too slow clotting occurs in the cannula.

Rauh, Cincinnati.

Body Temperature Variations in Apparently Healthy Children. F. van der Bogert and C. L. Moravec, J. Pediat. **10**:466 (April) 1937.

The authors observed the fluctuations in body temperature in normal children over a twenty-four hour period and found that the highest temperature occurred during the period from 11 a. m. to 3 p. m. When the hours of sleep were reversed, the temperature curve was reversed. Mental excitement caused slight but definite elevation of temperature in a fair proportion of the children. Oral temperature readings were taken for 500 school children during the early part of the morning, and 31.4 per cent of these children showed readings above 99 F. The percentage of girls showing a temperature above 99 F. was somewhat higher than that of boys. The children were divided into age groups, and of those in the 7 to 8 year group 43 per cent had a temperature above the accepted normal of 98.6 F. (oral). In the 9 to 13 year group 33 per cent reached the higher levels whereas in the group of children above 13 years of age only 8 per cent showed readings of 99 F. or above.

The authors conclude that the data collected confirm the clinical belief that slight elevations of temperature are compatible with health and that an oral reading slightly above 99 F. and a rectal reading slightly over 100 F. need not in the absence of other findings be considered evidence of disease.

Rauh, Cincinnati.

Elevated Temperatures in Childhood Due to Exercise. W. A. Hawke, J. Pediat. **11**:64 (July) 1937.

The temperature variations of thirty healthy children varying in age from 3 to 14 years and residing in a home for children with behavior problems were studied during two periods of twelve days each in February 1936 and in April 1936. Rectal temperatures were taken at 6 a. m. before rising, 11 a. m. before lunch, 4 p. m. before supper and 8 p. m. before retiring. In addition, the type of exercise and activity of the child during the hour or so before the temperature was taken was recorded. All children with infections were excluded from the study. The resting temperatures varied from 97.3 to 99.8 F., with an average of 98.2 F. After mild exercise the average temperature was 99.2 F., and the readings of 90 per cent of the children were above 99 F. After severe exercise the average reading was 100.2 F., and 70 per cent of the children had readings above 100 F. The highest reading obtained was 101.6 F., after a game of baseball. Every child showed some elevation of temperature after exercise, and in most instances the height depended on the activity of the child.

Rauh, Cincinnati.

THE USE OF PICROTOXIN AS AN ANTIDOTE FOR LUMINAL POISONING. S. J. COHEN and R. KOHN, J. Pharmacol. & Exper. Therap. **60**:102 (June) 1937.

The intravenous use of picrotoxin (131 mg. over forty-eight hours) seemed to be the determining factor in arousing a young woman deeply stuporous for three days from large doses of amytal and luminal, after other procedures had failed.

PILCHER, Cleveland.

STUDIES ON CALCIUM CREOSOTATE: II. THE "IN VITRO" COMPARATIVE STUDY OF THE EFFICIENCY OF CALCIUM CREOSOTATE, CALCIUM GUAIACOLATE AND CREOSOTE AS BACTERICIDAL AGENTS. III. THE ELIMINATION OF VOLATILE PHENOLS IN RABBIT URINE AFTER THE ADMINISTRATION OF "CALCIUM CREOSOTATE SOLUTION" AND AFTER CREOSOTE SOLUTION. E. J. FELLOWS, J. Pharmacol. & Exper. Therap. **60**:178 and 183 (June) 1937.

There is certain laboratory and clinical evidence that creosote and its compounds and derivatives have bactericidal properties. In the first paper Fellows concludes that "Calcium Creosotate Phenols 'in vitro' were shown to be effective bactericidal and bacteriostatic agents in higher dilutions than either creosote or calcium guaiacolate for the strains of B. coli communior, Staph. aureus and B. typhosus used."

In the second paper he gives evidence that the urine of rabbits contains more volatile phenols after administration of a calcium creosotate solution than after that of creosote and suggests that this indicates that the solution of creosotate is probably as well absorbed as creosote.

PILCHER, Cleveland.

ACTION OF P-AMINOBENZENESULFONAMIDE ON TYPE III PNEUMOCOCCUS IN MICE. F. B. COOPER, P. GROSS and R. R. MELLON, Proc. Soc. Exper. Biol. & Med. **36**:148 (March) 1937.

The oral administration of sulfanilamide (para-aminobenzenesulfonamide) succeeds in prolonging, and in some cases in saving, the lives of mice which had previously been infected subcutaneously with approximately ten minimal lethal doses of virulent type III pneumococci. The protection is not as great as that obtained in streptococcic or meningococcic infections. However, the authors believe that these experiments with mice justify a therapeutic trial of sulfanilamide in cases of infection with type III pneumococci in man.

HANSEN, Minneapolis.

COMPARISON OF PUNCTATE BASOPHILIA AND RATIO OF LARGE TO SMALL LYMPHOCYTES IN THE DIAGNOSIS AND PREVENTION OF LEAD POISONING. D. O. SHIELS, M. J. Australia **1**:535 (April 10) 1937.

Shiels affirms his previous report (*M. J. Australia* **1**:847 [June 20] 1936) that the magnitude of the ratio of large lymphoid cells to small lymphocytes is more closely related to the clinical condition in cases of lead poisoning than is the stippled cell count.

GONCE, Madison, Wis.

MEDICAL TRAINING IN THE U. S. S. R. E. H. CLUVER, South African M. J. **11**:369 (May 22) 1937.

First among the outstanding impressions gained by Cluver during a short visit to Russia was that the medical student is in an enviable position; he is a paid worker, with the privileges of a worker, which include, for example, access to the best seats in the theater and ballet. Cluver was also impressed with the suitability of introducing practical clinical work from the beginning of the course—not however, at the expense of scientific training, which is continued to the very end of the course. He noted, further, the extension of the usefulness of the doctors in the country by training of army surgeons and, lastly, the presence everywhere of women at the places where one went to learn about Russian medicine—at some places, to the complete exclusion of male doctors and students.

GONCE, Madison, Wis.

THREE TYPES OF INFANT AID. J. CHAUCHOY-WALTZ, Rev. méd.-sociale de l'enf. **5**:115 (March-April) 1937.

Chauchoy-Waltz feels that among the many forms of assistance employed in attempting to reduce infant mortality the following functioning "synergystically," offer the greatest promise: Properly organized nurseries, placement in families and milk dispensaries. For infants of certain types placement in a nursery is the only proper disposition, but the ever present danger of infection must be borne in mind. The mortality of as high as 33 per cent in some nurseries and the mention by Bohn-Nageotte in 1929 of "a satisfactory mortality of from 15 to 20 per cent" are quoted to stress this danger. The need for proper isolation (cubicle) and food in the nursery is discussed. The question of placement in a family is introduced with a brief review of the history of this type of social service. The supervision of the families, the care of the children, and the medical and nursing aid that must be given them are discussed. The recognized importance of breast milk stations is stressed, and a brief idea of facilities of this type throughout the world is presented.

DIETRICH, Beverly Hills, Calif.

THE MOTHER IN THE HOME. A. DOHRING, Rev. méd.-sociale de l'enf. **5**:134 (March-April) 1937.

This interesting paper calls attention to the frequency with which the ailing infant is deprived of home care because the mother and the father are both working, and hospitalization is the only solution. In one clinic 30 per cent of the infants were cared for by wetnurses, 30 per cent spent their days at nurseries, and only 40 per cent were really cared for by their mothers. Several illustrative case histories are cited. Although the author suggests that a dutiful mother, a father whose earnings are adequate, and a light and airy home are necessary for the realization of the ideal home situation for a sick child, he proposes no solution. [The value of home care for sick children has been emphasized by Brenneman in this country.—Abstractor.]

DIETRICH, Beverly Hills, Calif.

LYMPHATIC DIATHESIS. V. BAPTISTA, Arch. de pediat., Rio de Janeiro **9**:299 (July) 1937.

A discussion of status thymicolymphaticus and of adynamic lymphoidism (Pfaundler).

SANFORD, Chicago.

IDEA FOR A CHILDREN'S CONGRESS. S. DOBROWOLSKI, Zycie Dziecka **60**:65 (March) 1937.

The author presents an idea for a children's welfare congress; he emphasizes the necessity for it. Such a congress will be inaugurated in Poland for the first time.

The necessity for such action is great because there is no other age in life so neglected as that of childhood, particularly in poor countries. The problem for discussion should be the public's obligation to the child and the life of the child in the light of its necessity. Care for the child should be the greatest of life's obligations.

KRUPINSKI, Chicago.

Book Reviews

The Care and Feeding of Babies in Warm Climates. By Charles James Bloom, M.D. Price, $2.75. Pp. 346, with 45 illustrations. New Orleans: Pelican Publishing Company, 1937.

This book of 346 pages has been prepared by a pediatrician in order to help the mother understand the needs and care of the new-born and of the older infant. Beginning with some advice to the mother on antepartum precautions, the author skilfully presents the attributes of the average baby, gives pertinent advice on the selection of a nurse and describes in detail care in the nursery and routine in the home. He outlines the general types of feeding; discusses first aid, general measures for the sick infant and practical medical procedures, such as enemas and inhalations, and offers advice on habits and training.

One of the most helpful features of the book is a chapter on recipes for the child in early years. The name of the book is slightly misleading because it applies equally well to babies in temperate climates.

Directory of Pediatric Societies*

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Herreplein, Groningen, Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Prof. Luigi Spolverini, Policlinico Lungo Tevere Melini 24, Rome, Italy.
Secretary: Professor Vitetti, Rome, Italy.
Place: Boston. Time: Summer and Fall, 1940.
American Committee:
Chairman: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Kenneth Blackfan, 300 Longwood Ave., Boston.
Canadian Committee:
Chairman: Dr. H. B. Cushing, 1390 Sherbrooke St., W., Montreal.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St., W., Montreal.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

British Paediatric Association

President: Dr. J. Wilkie Scott, 40 The Rope Walk, Nottingham, England.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

Royal Society of Medicine, Section for the Study of Diseases in Children

President: Dr. T. Twistington Higgins, 12 Queen Anne St., London, W. 1.
Secretary: Dr. Reginald Lightwood, 86 Brooke St., London, W. 1.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:30 p. m.

Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv, Palestine.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv, Palestine.

Sociedad Cubana de Pediatría

President: Prof. Félix Hurtado Galtés, Carlos III 7, Habana.
Secretary: Dr. Carlos Hernández Miyares, San Lazaro 370, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Third Thursday of every month.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Clifford D. Sweet, 2940 Summit St., Oakland, Calif.
Secretary: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Place: San Francisco. Time: June 13-17, 1938.

American Academy of Pediatrics

President: Dr. Philip Van Ingen, 125 E. 71st St., New York.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: Del Monte Hotel, Del Monte, Calif. Time: June 9-11, 1938.
Region I. Place: Rochester, N. Y.
Region III. Place: Detroit, Mich.

American Hospital Association, Children's Hospital Section

Chairman: Miss Mabel Binner, Children's Memorial Hospital, Chicago.
Secretary: Winifred Culbertson, Children's Convalescent Hospital, Cincinnati.

American Pediatric Society

President: Dr. Kenneth D. Blackfan, 300 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: Berkshire Inn, Great Barrington, Mass. Time: May 5-7, 1938.

Canadian Society for the Study of Diseases of Children

President: Dr. Alton Goldbloom, 1543 Crescent St., Montreal, Quebec.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.

Society for Pediatric Research

President: Dr. Samuel Z. Levine, 525 E. 68th St., New York.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

North Pacific Pediatric Society

President: Frederick Fischer, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. C. L. Lyons, Paulsen Medical-Dental Bldg., Spokane, Wash.
Place: Seattle. Time: Last Saturday in January 1938.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Gilbert Levy, 20 S. Dunlap St., Memphis, Tenn.
Secretary: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.

STATE

Alabama Pediatric Society

President: Dr. J. H. Baumhauer, 56 St. Joseph St., Mobile.
Secretary-Treasurer: Dr. M. Vaun Adams, 803 Government St., Mobile.
Place: Mobile. Time: Third Monday in April 1938.

Arkansas State Pediatric Association

Chairman: Dr. E. C. McMullen, 500 Main St., Pine Bluff.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.
Place: Texarkana, Ark. Time: February 1938.

California State Medical Society, Section on Pediatrics

Chairman: Dr. E. Earl Moody, 3780 Wilshire Blvd., Los Angeles.
Secretary: Dr. Hartzel H. Ray, 23-2d Ave., San Mateo.
Place: Pasadena. Time: May 9-12, 1938.

Florida State Pediatric Society

President: Dr. Douglas D. Martin, 442 W. Lafayette St., Tampa.
Secretary: Dr. Warren W. Quillian, 227 Avenue Aragon, Coral Gables.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St., N. E., Atlanta.
Place: Augusta. Time: April 1938.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. J. Harold Root, 103 N. Main St., Waterbury.
Secretary: Dr. Joseph L. Hetzel, 103 N. Main St., Waterbury.
Time: Three meetings a year.

Indiana State Pediatric Society

President: Dr. Ernest R. Carlo, 2902 Fairfield Ave., Fort Wayne.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

Louisiana State Pediatric Society

President: Dr. Clarence H. Webb, 624 Travis St., Shreveport.
Secretary-Treasurer: Dr. Ruth Aleman, 1407 S. Carrollton Ave., New Orleans.
Place: New Orleans. Time: April 25-27, 1938.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. John D. Craig, 33 E. 61st St., New York.
Secretary: Dr. Norman L. Hawkins, 11 Public Sq., Watertown, N. Y.
Place: New York. Time: May 9-12, 1938.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. John P. Scott, 1740 Bainbridge St., Philadelphia.
Secretary: Dr. John M. Higgins, 600 S. Wilbur Ave., Sayre.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.
Secretary: Dr. Ward Chadwick, 524 Medical Arts Bldg., Grand Rapids.

Mississippi State Pediatric Society

President: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Secretary-Treasurer: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Place: To be designated by Society. Time: Yearly.

Nebraska Pediatric Society

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. John LaBruce Ward, Arcade Bldg., Asheville.
Secretary: Dr. Lewis Elias, 36 Grove St., Asheville.

Oklahoma State Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. Ben H. Nicholson, 301 W. 12th St., Oklahoma City.

South Carolina Pediatric Society

President: Dr. Leland B. Salters, 317 S. Warley St., Florence.
Secretary-Treasurer: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. Eugene Rosamond, 1074 Madison Ave., Memphis.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Place: Nashville. Time: April 12-14, 1938.

TEXAS PEDIATRIC SOCIETY

President: Dr. John G. Young, 3930 McKinney Ave., Dallas.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Galveston. Time: May 10-12, 1938.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. W. Ambrose McGee, 616 W. Grace St., Richmond.
Secretary: Dr. John M. Bishop, Medical Arts Bldg., Roanoke.
Place: Danville, Va. Time: October 1938.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.
Secretary: Dr. Theresa O. Snaith, Weston.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Secretary: Dr. Arthur J. Horesh, 10515 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. T. B. Verner, 170 St. George St., Toronto.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto.

BRONX PEDIATRIC SOCIETY

President: Dr. Samuel Tripler, 1555 Grand Concourse, New York.
Secretary: Dr. Harry S. Altman, 940 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

BROOKLYN ACADEMY OF PEDIATRICS

President: Dr. Walter D. Ludlum, 1421 Cortelyou Rd., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vasder Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

CHICAGO PEDIATRIC SOCIETY

President: Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.
Secretary: Dr. George F. Munns, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave., Chicago. Time: Third Tuesday of each month, October to May, inclusive.

DALLAS PEDIATRIC SOCIETY

President: Dr. John Young, 3930 McKinney Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3622 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. W. J. Scott, 5140–2d Ave., Detroit.
Secretary: Dr. Harold E. Clark, 100 Atkinson Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. T. F. Davenport, 104 Ponce de Leon Ave., Atlanta.
Secretary: Dr. James P. Hanner, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Walter F. Qualtrough, 920 Westheimer Ave., Houston, Texas.
Secretary-Treasurer: Dr. Allan Penny Bloxsom, 4402 Travis St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 1020 Boston Bldg., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. W. R. Moore, 620 Francis St., St. Joseph.
Secretary: Dr. F. S. Hogue, 1103 Grand Ave., Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Edwin F. Patton, 3875 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Henry F. Gallagher, 1930 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Harry R. Litchfield, 163 Eastern Parkway, Brooklyn.
Secretary: Dr. Jacob Rosenblum, 550 Ocean Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. W. C. A. Steffen, 42 Union St., Flushing, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144–38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May

Memphis Pediatric Society

President: Dr. Clyde V. Croswell, 1052 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. David W. Goltman, 1073 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. Joseph Shimpa, 2309 N. 36th St., Milwaukee.
Secretary: Dr. Helen Jane Zillmer, 781 N. Jefferson St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Henry E. Utter, 122 Waterman St., Providence, R. I.
Secretary-Treasurer: Dr. Henry E. Gallup, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Samuel Z. Levine, 525 E. 68th St., New York.
Secretary: Dr. Philip M. Stimson, 25 Claremont Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Roger L. J. Kennedy, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Robert Rosenthal, 437 Lowry Medical Arts Bldg., St. Paul.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Oklahoma City Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Time: Alternate months.

Philadelphia Pediatric Society

President: Dr. Julian M. Lyon, 40 Llanfair Rd., Ardmore, Pa.
Secretary: Dr. Aims C. McGuinness, Children's Hospital, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. A. S. Hurt, 1028 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. Louise Fry Galvin, 2416 Stuart Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

Rochester Pediatric Society

President: Dr. J. Merrel Parker, 11 N. Goodman St., Rochester, N. Y.
Secretary: Dr. H. C. Soule, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

Rocky Mountain Pediatric Society

President: Dr. James E. Russell Jr., 820 Metropolitan Bldg., Denver.
Secretary: Dr. F. Craig Johnson, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. John Zahorsky, 536 N. Taylor Ave., St. Louis.
Secretary-Treasurer: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Frank H. Douglass, Medical Dental Bldg., Seattle.
Secretary: Dr. C. Luverne Smith, Stimson Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Louis M. Earle, 6381 Hollywood Blvd., Los Angeles.
Secretary: Dr. Philip E. Rothman, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. Damon O. Walthall, 1103 Grand Ave., Kansas City, Mo.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (NEW YORK)

President: Dr. R. A. Higgons, 264 King St., Port Chester, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 131 Purchase St., Rye, N. Y.
Place: Grasslands Hospital. Time: Third Thursday in October, December, February and April.